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SAVE THE DATE

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Details to follow

Mission Statement:

To advance the profession of pharmacy, enabling our members to provide optimal care to those they serve.

President's Letter

Hi Everyone! It was wonderful seeing you all at this year's convention in Asbury Park! I had a great time at our sessions, social activities and chatting with you in the halls – I hope you agree!

I am proud to say that we had our Second Annual Poster Session, with double the posters than what were presented last year – this is a great accomplishment! Our vendors were pleased with the interactions they had with all of you and are looking forward to joining us again next year. The student programming was, yet again, a successfully executed and action packed day for the future of our profession. Lastly, I'd like to mention the successful Compounding Essentials Course that was developed and delivered by NJPhA at this year's convention. Let's continue making strides for our Profession!

My vision for the upcoming year.

So, what does the upcoming year look like for us? Our main purpose will be to continue to advocate on behalf of all the Pharmacists and Pharmacy Technicians in the State of New Jersey. Our focus continues to be obtaining provider status for Pharmacists – if passed, under the Affordable Care Act this would allow pharmacists to bill and be paid for services rendered.

Our Advocacy Team actively works with APhA – American Pharmacists Association, NASPA – National Alliance of State Pharmacy Associations, NCPA – National Community Pharmacists Association and others to protect our best interests and promote grassroots federal advocacy on key issues. It is not enough to only influence law changes, we must also influence regulations in order to impact change – our team works with the NJ Board of Pharmacy, Board of Medical Examiners, Drug Utilization Review Board, Health Information Technology Committee, NABP – National Association of Boards of Pharmacy, APhA and the Center for Medicare & Medicaid Services (CMS) to make law updates a reality for pharmacists in every day practice.

In addition to working hard on Advocacy, I have asked our Leadership Team to continue to take an active role in strengthening our Association through a variety of events and opportunities for our members. Welcome and thank you to all of our new and continuing leadership members – your hard work and dedication is much appreciated!

If you are interested in learning more or becoming a more active member, please reach out to anyone in Leadership or in the office!

Sincerely

Moriah
Moriah Weissman, PharmD, CCP

From The Editors' Desks...

Dear Colleagues,

I hope this issue finds you healthy and happy, and enjoying the summer. We are pleased to present our Fall 2014 issue, focusing on infectious diseases (ID). Practicing pharmacists are managing patients who are at one time or another on an anti-infective, so the relevance of this topic spans across most practice settings. This issue introduces a new antibiotic, dalbavancin, in which you can earn free continuing education credit. The growing incidence of *C. diff* infections in pediatric populations is also presented, and once again, the Ohio Pharmacists Foundation, Inc., has shared timely continuing education activities with our organization.

In this issue, we highlight poster presentations from our Annual Convention in Asbury Park, NJ (September 19 – 21, 2014.) We also congratulate our Practice Spotlight practitioner on an impressive award!

The theme of the next issue is endocrinology. Please consider writing a piece for inclusion (deadline Sept. 8). In utilizing the vast knowledge of the practitioners in our organization, we can have an amazing resource in our quarterly Journal! Please email ideas and submissions to leibfried2@hotmail.com or rutu.p.parikh@gmail.com. We will help you come up with a topic if you are stumped!

Happy reading! Enjoy the convention photos, too!

Regards,
Maria Leibfried, BS, PharmD, BCNSP, CCP
Rutu Patel, PharmD
Co-editors

Message from the CEO

What a Difference a Volunteer Makes!

As you can imagine, organizing, preparing for, and running a statewide convention is no small task. The NJPhA office staff jumps into action by later spring but…did you know how many volunteer hours are contributed to NJPhA before then?

The Convention Committee barely returns the suitcase to the closet, when planning for the next convention begins. Venue, topics, speakers, exhibitors, networking, activities, and nightlife—are all under their charge! They are not the only volunteers involved, though. As topics are suggested, the Continuing Education Committee assists in identifying presenters, and reviewing the slide decks and related material against the ACPE guidelines before accreditation can take place. The Student Practitioner Committee coordinates the student activities and programming for the Student Track. In addition, students and faculty advisors dedicate many hours to organizing the Student Pharmacists Self Care Championship, recruiting college teams and enlisting the help of moderators and judges. It is a huge volunteer effort, and we are grateful to every one of them.

When the behind-the-scenes work is complete, the office picks up the various items and pushes them to the finish line doing, well, all the things an office does before a convention!

As the convention nears, student volunteers get more involved in the office, and they asked to do things from designing notices in the publisher program, uploading presentations on laptops, to packing boxes to ship to the convention venue. While on site at the convention, they assist with registration, hook up AV for presenters, and they make themselves readily available for any task.

Volunteering at NJPhA is not limited to convention activities. Your interests and expertise can be matched to a number of NJPhA committees. You can find an outline of each committee on our website. Email an inquiry about serving as a committee member through the online link, or call the office and I will be happy to answer your questions. Leadership positions are also volunteer opportunities where your passion and expertise meld perfectly! Consider participating as a regional leader or a state officer.

Through engagement, one begins the see what a difference a volunteer makes to an organization. Volunteers benefit the membership through their efforts to assist NJPhA with projects and tasks that a small staff would struggle to add to daily administrative duties.

It is not all work (it can be fun too!), but it is a dedicated community of professionals that want to help advance the profession of pharmacy.

Will you be a volunteer in 2015?
Please do!

Elise M. Barry

Message from the BOT Chairman

Dear NJPhA Members,

Now exactly one month since our Annual Convention in Asbury Park, NJ the days are getting short and the weather crisp. We hope you enjoyed some of the new features of Convention this year, including our professional development sessions and our sponsored dinner where we discussed health care reform. For me the most fun, by far, was our Student Competition. Packed to the gills with pharmacists that struggled to keep their suggestions quiet, the room was filled with school pride as well as pharmacy pride. And speaking of pride, the activity that I felt the most pride about was the poster session. Doubled in size from last year when we re-instated it after many years, this session brings diversity to our meeting in content and ups the professionalism of the overall meeting. My sincere thanks to those who submitted posters, for their research and for participating in the meeting, answering questions and representing the value of pharmacists in yet another way. Finally, the most touching moment for me came during the awards ceremony. Of course, it is a privilege to shake the hands of these amazing people, and all recipients were very appreciative of their recognition. For me, though, the most poignant moment was when Ivan Saiff accepted the Rosario (Russ) Mannino award. As an award committee member, I knew the impressive credentials that won Ivan this recognition. What I could never know, until that day, was how much this award would mean to Ivan - that Russ and his wife were people that meant so much to Ivan and to be recognized with this award was particularly moving.

I hope you each had similar moments, in addition to achieving the education you wanted.

As we hurtle into the end of the year and all the extra busy-ness that entails, I wish you a happy and healthy remainder to 2014 and implore you to keep NJPhA strong with your membership renewal for 2015.

Kind regards,
Carrie

The Gut Problem with Community-Acquired "Clostridium Difficile" Infections Among Pediatric Patients

By Brian J. Catton, PharmD

INTRODUCTION

Since Andrew Fleming discovered penicillin in 1928, antibiotics have been one of the most influential medications in the history of medicine. Thanks to its discovery, many American and British soldiers were saved during World War II from pneumonia and wound infections caused during combat. Penicillin began the exciting quest to create other antibiotics to treat various infections, but also began the threats of antibiotic resistance and virulence. As important as resistance is, antibiotics have shown their concerning side effects and adverse drug events (ADEs). The pediatric population is highly susceptible and vulnerable to them.

According to the Centers for Disease Control and Prevention (CDC), one out of five emergency department visits is due to ADEs from antibiotics. In pediatric patients, antibiotics are the most common cause of ADE emergency department visits. In 2013, the CDC published their classification of bacteria based on specific hazard levels due to their resistance and/or virulence, with *Clostridium difficile* infections (CDIs) listed as "urgent". Although CDIs have not shown significant drug resistance, CDIs result annually in 250,000 infections, 14,000 deaths, and one billion dollars in excess medical costs annually. Although seen predominately in adults and the elderly, CDIs are beginning to infect the pediatric population. In the pediatric population, 71% of children in a CDC-conducted study acquired CDIs in the community; 73% of those children were on antibiotics during the 12 weeks prior to their illness. By raising awareness of CDIs in the pediatric population, pharmacists can take appropriate measures to reduce incidence, cost, and mortality of CDIs among the youngest of all patients.[1]

CLOSTRIDIUM DIFFICILE AND COLONIC CELLULAR APOPTOSIS

Clostridium difficile (C. diff) is a spore-forming Gram-positive bacillus, obligate anaerobe most commonly transmitted via the fecal-oral route[2]. *C. diff* produces several toxins, mainly toxins A & B, via genetic translation within the bacterium's nucleus. Although toxins A & B are very pathogenic, they are also easily detected through testing. Once toxins A & B are produced, they enter intestinal cells through receptor-mediated endocytosis and are then translocated to the cytosol via acidified endosomes. After binding onto and inactivating small GTPases, inactivation and enzymatic modification via glycosylation results.

Enzymatic modification via toxins A & B most commonly results in decreased actin production, thereby compromising intracellular integrity. In addition to disrupting cellular structure, the toxins enhance inflammatory events by increasing colonic epithelial permeability. Additionally, the toxins indirectly activate several cytokines and chemokines in intestinal epithelial cells, and kinases in monocytes, resulting in increasing access for polymorphonuclear cells into damaged, colonic epithelial cells. These processes ultimately lead to colonic cellular apoptosis. Additional mechanisms of colonic cellular apoptosis include, but are not limited to, the following:

- Mitochondrial disruption and modulation of substance P activation, resulting in production of tumor necrosis factor alpha; and
- Disruption of tight junction formations between colonic epithelium via inactivating Rho proteins, thus allowing neutrophils to migrate into the intestines and accumulate.[3]

RISK FACTORS

Risk factors for *C. diff* infections include gastrointestinal surgery (including gastrostomy or jejunostomy tubes), prolonged stays at healthcare facilities, chronic immunosuppressive conditions (e.g. solid organ transplant, hematologic/oncologic conditions), immunosuppressive medications (e.g. chemotherapy, corticosteroids), and proton-pump inhibitor therapy[2]. The greatest risk factor involves recent antibiotic therapy with fluoroquinolones, clindamycin, broad-spectrum penicillins (e.g. amoxicillin/clavulanic acid), or broad-spectrum cephalosporins (e.g. cefuroxime)[4].

CLINICAL MANIFESTATIONS

Symptoms of CDIs, which may develop upon 6 weeks after antibiotic discontinuation, range from asymptomatic colonization to life-threatening disease. Although once regarded to be asymptomatic carriers, neonates and infants have been diagnosed with diarrhea due to CDIs[6]. Symptomatic children may experience watery diarrhea, fever, loss of appetite, or abdominal pain[7]. *Clostrodium difficile*-associated diarrhea (CDAD) may include watery diarrhea, pseudomembranous colitis, toxic megacolon, perforation, and bacteremia. Due to the colonic damage caused by toxins A & B, pesudomembranes may line the colonic mucosa. In severe CDI cases, toxic megacolon can be exacerbated by electrolyte loss from watery diarrhea. Signs and symptoms of toxic megacolon include partial or complete colonic dilation, fever, leukocytosis, tachycardia, dehydration, and altered mental status. Colonic perforation leads to the influx of inflammatory cells, resulting in the production of a phlegmon within the colonic connective tissue. This can cause osmotic imbalance, generalized sepsis, bacteremia, and shock.[2]

DIAGNOSIS

Collecting an unformed stool sample is the cornerstone for properly diagnosing CDIs. Although cell culture cytotoxicity neutralization assay (CCNA) was once highly regarded due to 75-90% sensitivity and 95-100% specificity, CCNA is now obsolete due to slow turnaround time and high labor demand[7]. The most accurate testing used to diagnose CDIs is polymerase chain reaction

(PCR) assay for toxins A and B. Even though PCR is costly, its 95% sensitivity and 100% specificity results in rapid discontinuation of contact isolation and inappropriate antibiotics, ultimately resulting in decreased hospitalized stays[5,7]. Currently, routine CDI testing in neonates and infants is not recommended. In children ages one to three years, testing is recommended in children with diarrhea after ruling out other causes of diarrhea. Testing in children older than three years of age can be conducted in the same manner as adults[5,7].

TREATMENT

Treatment among the pediatric population involves supportive care, discontinuing CDI-causative agents, and initiating anti-CDI therapy. Intravenous hydration therapy is recommended to treat dehydration and restore proper electrolyte levels. Antispasmodic agents (e.g. diphenoxylate) are strongly discouraged due to *C. diff* toxin buildup. In mild CDI cases, oral metronidazole is recommended at 30 mg/kg/day in four divided doses (maximum, 2 gm/day); moderate to severe cases require oral vancomycin at 40 mg/kg/day in four divided doses (maximum 2 gm/day) with or without oral metronidazole. Although 20-30% of CDIs result in future recurrence following their initial episode, a second course of the same antibiotic therapy is recommended; should that fail, then pulsated oral vancomycin therapy is recommended[5,7].

Other anti-CDI therapy includes nitazoxanide and fidaxomicin. The University of Michigan Department of Pediatrics conducted a study to determine whether nitazoxanide is more effective than oral metronidazole in treating hospitalized children with pseudomembranous colitis. Oral metronidazole and nitazoxanide both demonstrated a similar response, although the sample size was small.[8] Fidaxomicin has proven to as effective as oral vancomycin in treating CDIs in adults due to its minimal systemic absorption, excellent safety profile, and lower recurrence rate; however, efficacy in children is still to be determined[5,7].

PREVENTION

The most effective way to prevent the spread of CDIs is hand washing with soap and water. Other preventative measures include contact isolation (e.g. using separate bathrooms), decontaminating contact surfaces with sporicidal cleaning agents, and wearing gloves around patients with CDIs[1,4,7]. Proper antimicrobial stewardship programs can be utilized to not only prevent the spread of CDIs but also treat current infection.

The CDC is a resource for healthcare providers and patients. Measures can be taken to reduce CDIs, potentially saving 20,000 lives, preventing 150,000 hospitalizations, and cutting up to two billion dollars in healthcare costs annually[9]. Lauri Hicks, DO, director of the CDC program Get Smart: Know When Antibiotics Work, mentions, "I know how difficult it is to see your child suffer with something … [but] antibiotics aren't always the answer."

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Dalbavancin, a once-weekly treatment for Acute Bacterial Skin and Skin Structure Infections

by Rebecca Yu, PharmD

0.5 credit hour UAN: 0136-0000-14-049-H04-P
Knowledge based activity UAN: 0136-0000-14-049-H04-T

Learning Objectives:
After participating in this activity, the pharmacist shall be able to:
1. Describe the role of dalbavancin in the treatment of adults with acute bacterial skin and skin structure infections
2. Discuss the two most recent clinical trials evaluating the efficacy and safety of dalbavancin
3. List the 6 most common side effects of dalbavancin
4. Recommend the appropriate dose and route of administration for an appropriate patient
5. Describe the proper medication preparation procedure

After participating in this activity, the pharmacy technician shall be able to:
1. Describe the general pharmacologic class of dalbavancin
2. Describe the type of infections for which dalbavancin is approved
3. Name the most common side effect of dalbavancin
4. Name the appropriate diluent for reconstituting dalbavancin
5. Describe the storage requirements and stability of reconstituted dalbavancin

On May 23, 2014 dalbavancin became the first drug to be approved as a qualified infectious disease product (QIDP). QIDP is a designation created by the Generating Antibiotic Incentives Now (GAIN) title of the Food and Drug Administration's Safety and Innovation Act (FDASIA) passed in 2012, in an effort to counteract the growing threat of antimicrobial resistance. Dalbavancin, which is marketed under the trade name Dalvance® by Durata Therapeutics, was approved for the treatment of adults with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible and resistant gram-positive bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA).[1]

Pharmacology
Dalbavancin is a semisynthetic lipoglycopeptide, derived from a compound produced by the *Nonomuria* species of actinomyces.[2] It binds to the C-terminal D-alanyl-D-alanine to prevent peptidoglycan polymerization and cross-linking, thus inhibiting cell wall synthesis and consequently causing cell death.3 Dalbavancin has a long lipophilic side chain, which enhances its antimicrobial activity by increasing its affinity for the D-Ala-D-Ala terminal and also increases the half-life.[2]

Pharmacokinetics
Dalbavancin exhibits dose-dependent, linear pharmacokinetics most nearly demonstrated by a two-compartment model with first-order elimination.[4]

Absorption Dalbavancin has poor oral bioavailability and is available for IV administration only.

Distribution C_{max} is achieved immediately at the end of infusion. Administration of a 1000 mg dose resulted in a steady-state volume of distribution ranging from 0.14 L/kg to 0.18 L/kg. Approximately 93% of dalbavancin is reversibly protein-bound primarily to albumin. Steady-state concentrations are reached within two to three days of initiation.[5]

Metabolism Dalbavancin is not known to be a substrate, inhibitor, or inducer of cytochrome P450 (CYP450) isoenzymes. Hydroxy-dalbavancin and mannosylaglycone, two metabolites, can be detected in the urine but are marginally or not detectable in the plasma and do not contribute to the *in vivo* activity of dalbavancin. AUC_{0-336} hrs was decreased by 28% to 31% in subjects with moderate to severe hepatic impairment compared with those with normal hepatic function. The clinical relevance of this decrease is unknown, and caution is recommended when administering dalbavancin to patients with moderate to severe hepatic impairment.[6]

Excretion Dalbavancin is eliminated renally and nonrenally and has a half-life ranging from 149 to 198 hours. Approximately 33% of the drug is excreted unchanged in the urine, while 20% is eliminated through feces.[7] No dosage adjustments are recommended for patients with creatinine clearance (CrCl) greater than 30 mL/min or on hemodialysis. For patients with CrCl less than 30 mL/min, not receiving hemodialysis, the recommended regimen is 750 mg IV then 375 mg IV one week later.[6]

Spectrum of Activity
Dalbavancin is active against gram-positive bacteria, such as methicillin-sensitive and resistant S.aureus (MRSA), streptococci, and enterococci, including VanB type enterococci.[8]

For most species of aerobic gram-positive organisms studied, the minimum inhibitory concentration observed in *in vitro* studies for at least 90% of the strains (MIC_{90}) ranged from 0.03 to 0.12 mcg/mL.[8] Consequently, the susceptibility breakpoint was set at 0.12 mcg/mL.[6] Below this breakpoint, organisms are considered susceptible to dalbavancin. In *in vitro* studies, some strains of *s. agalactiae,* penicillin-resistant *s. pneumoniae, e. faecalis,* and *e. faecium* had MICs greater than the susceptibility breakpoint.[8] Due to insufficient data, intermediate susceptibility and resistance breakpoints have not been set.

Clinical Efficacy
The two most recent phase III trials evaluating dalbavancin are commonly referred to as DISCOVER 1 and DISCOVER 2 trials.

The DISCOVER 1 and DISCOVER 2 trials were identical double-blind, double-dummy, multicenter, international, non-inferiority trials designed to evaluate the efficacy of dalbavancin compared with vancomycin with an optional switch to linezolid in the treatment of ABSSSI. A combined total of 1312 patients was randomized in a 1:1 ratio to the treatment arms shown in **figure 1**.[9] A pharmacist was permitted to adjust vancomycin doses in accordance with local standards of care. Inclusion criteria were as follows on next page.

Figure 1

Dalbavancin arm	Vancomycin/Linezolid arm
Day 1	**Days 1-3**
Dalbavancin 1000 mg IV over 30 minutes once	Vancomycin 1000 mg IV q12h or Vancomycin 15 mg/kg IV q12h
Day 8	**Days 4-14**
Dalbavancin 500 mg IV over 30 minutes once	Vancomycin 1000 mg IV q12h or Vancomycin 15 mg/kg IV q12h or Linezolid 600 mg PO q12h

- Age ≥ 18
- Diagnosis of ABSSSI with the presence of cellulitis, major abscess, or wound infection associated with at least 75 cm2 of erythema
- Expected to require at least 3 days of intravenous therapy
- One or more systemic signs of infection within 24 hours of randomization
- Temperature >38˚C
- White blood cell count >12,000/mm3 or bands >10%

Patients were excluded if they had received antibiotics within 14 days of randomization. Patients were well-randomized in regard to age, sex, and race.[9] However, there were more subjects with diabetes mellitus in the vancomycin/linezolid groups (14.1%) compared with the dalbavancin groups (11.8%).

The primary endpoint was measured at 48 to 72 hours and treatment success was defined as both cessation of spread of infection-associated erythema and temperature of <37.6˚C at three consecutive readings taken 6 hours apart. In the pooled analysis of the intent-to-treat population, 79.7% and 79.8% (weighted difference -0.1%, 95% CI -4.5 to 4.2) in the dalbavancin and vancomycin/linezolid groups, respectively, achieved early clinical response.[9]

Safety and tolerability

The number of patients experiencing treatment-related adverse events was similar in both arms. The most common adverse events associated with dalbavancin were nausea (2.5%), diarrhea (0.8%), and pruritus (0.6%). In DISCOVER 1 and 2, adverse events led to discontinuation in 2.1% and 2.0% of dalbavancin and vancomycin/linezolid patients, respectively.9 The percentage of patients experiencing adverse events in DISCOVER 1 and 2 was lower than in other Phase 2 and Phase 3 trials. In other trials, nausea (5.5%), vomiting (2.8%), diarrhea (4.4%), headache (4.7%), rash (2.7%), and pruritus (2.1%) were the most common adverse reactions.[6]

Dosing and Administration[9]

The usual dose of dalbavancin is 1000 mg infused intravenously over 30 minutes, followed by a 500 mg dose also infused over 30 minutes one week later. It is supplied in single-use vials containing 500 mg of anhydrous dalbavancin powder for reconstitution. Each vial of dalbavancin should be reconstituted with 25 mL of sterile water for injection, USP, to yield a clear to yellow solution containing 20 mg/mL of dalbavancin. The medication should then be diluted to a concentration of 1 mg/mL to 5 mg/mL by transferring the reconstituted solution, using aseptic technique, to an appropriately sized bag or bottle of 5% dextrose injection, USP. Saline solutions may cause precipitation and should not be used. Solutions of dalbavancin can be stored in the refrigerator (2 to 8˚C) or at controlled room temperature (20 to 25˚C), but should be administered within 48 hours of reconstitution.

Conclusion

Dalbavancin is a safe and non-inferior alternative to vancomycin for the treatment of ABSSSIs caused by gram-positive organisms. The primary advantage of dalbavancin is its two-dose regimen, which has the potential to reduce length of stay in certain patients. A reduced length of stay could mitigate the effect of the higher acquisition cost. Although resistance to dalbavancin was not reported in clinical trials, *in vitro* studies have shown resistance of vanA type enterococci to dalbavancin. The clinical utility of dalbavancin in patients with vancomycin-resistant infections has yet to be determined.

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Continuing Education Quiz:

The New Jersey Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program is approved for a maximum of 1/2 hour (0.05 CEU) of pharmacy continuing education credit. A Statement of Credits will be issued within 30 days subject to documented completion of tests and evaluation materials. Expiration Date: 11/01/2017
UAN: 0136-0000-14-049-H04-P; 0136-0000-14-049-H04-T Dalbavancin, a once weekly treatment for Acute Bacterial Skin and Skin Structure Infections

Pharmacist Post Test

1. Dalbavancin is indicated for use in
   a. adults b. children c. neonates
2. Dalbavancin is indicated to treat the following type of infections:
   a. uncomplicated urinary tract
   b. acute viral endocarditis
   c. acute bacterial skin and skin structure infections
   d. chronic hepatitis C
3. Dalbavancin is active against
   a. streptococci, E. coli, H. influenza
   b. MRSA, H. influenza, hepatitis C
   c. enterococcus, streptococci, MRSA
   d. E. coli, enterococcus, MSSA
4. The DISCOVER 1 and DISCOVER 2 studies
   a. compared dalbavancin to vancomycin (with an optional switch to linezolid)
   b. enrolled over 3000 patients
   c. evaluated the safety of dalbavancin in children ages 6 – 12 years
   d. found that dalbavancin was superior to other antibiotics
5. The most common side effects with dalbavancin are
   a. alopecia, blurry vision, headache, pruritis, rash, diarrhea
   b. constipation, nausea, vomiting, diarrhea, anuria, headache
   c. nausea, vomiting, diarrhea, headache, rash, pruritis
   d. elevated LFTs, vomiting, rash, amenorrhea, azotemia, nausea
6. What is the appropriate intravenous dose for an adult with normal renal function and with an acute bacterial skin infection with MRSA?
   a. 2 gram IV daily x 14 days
   b. 500 mg IV once a week x 6 weeks
   c. 1 gram IV followed by a 500 mg dose one week later
   d. 1200 mg IV q6h x 4 doses
7. The route of administration for dalbavancin is [SELECT ALL THAT APPLY]
   a. IV c. PO
   b. IM d. SQ
8. A 1 gram dose of dalbavancin should be administered
   a. IV push c. over 30 minutes
   b. over 10 minutes d. over 60 minutes
9. Dalbavancin is available as
   a. an anhydrous powder for reconstitution
   b. a premixed IV solution
   c. a liquid medication in an ampule
   d. a prefilled syringe
10. In order to make the highest concentration of the final solution, after reconstitution with 25 ml of sterile water for injection, dalbavancin 1 gram is to be prepared in
    a. 50 ml of D5W c. 50 ml of NS
    b. 200 ml of D5W d. 200 ml of NS

Pharmacy Technician Post Test

1. Dalbavancin is indicated for use in
   a. adults b. children c. neonates
2. Dalbavancin is
   a. an antiarrhythmic b. a corticosteroid c. an antibiotic
3. Dalbavancin is active against
   a. fungi b. viruses c. bacteria
4. Two studies that evaluated the safety and efficacy of dalbavancin are the
   a. DISCOVER 1 and DISCOVER 2 studies
   b. LEARN 4 and LEARN 5 studies
   c. TIMI 2 and TIMI 3 studies
5. According to the 2 most recent studies, a common side effect with dalbavancin is
   a. blurry vision b. constipation c. nausea
6. Which dose is a typical dose that would appear on an order for dalbavancin?
   a. 250 mg IV Q12 hours
   b. 500 mg IV daily x 10 days
   c. 1000 mg IV x 1 dose followed by 500 mg IV one week later
7. The route of administration for dalbavancin is [SELECT ALL THAT APPLY]
   a. IV b. PO c. SQ
8. A 1 gram dose of dalbavancin should be administered
   a. IV push c. over 30 minutes
   b. over 10 minutes d. over 60 minutes
9. Dalbavancin is available as
   a. an anhydrous powder for reconstitution
   b. a premixed IV solution
   c. a liquid medication in an ampule
   d. a prefilled syringe
10. In order to make a solution with a final concentration of 5mg/ml, after reconstitution with 25 ml of sterile water for injection, dalbavancin 1 gram is to be prepared in
    a. 50 ml
    b. 200 ml
    c. 500 ml
    d. 1000 ml

Program Evaluation – Must be completed for credit
Please rate the following items on a scale from 1 (poor) to 4 (excellent).

1. Overall quality of the article	1	2	3	4
2. Relevance to pharmacy practice	1	2	3	4
3. Value of the content	1	2	3	4

Please answer if you agree or disagree
4. The program met the stated learning objectives: ☐ Agree ☐ Disagree

Impact of the Activity

5. The information presented (check all that applies):
   ☐ Reinforced my current practice/treatment habits
   ☐ Will improve my practice/patient outcomes
   ☐ Provided new ideas or information I expect to use
   ☐ Adds to my knowledge
6. Will the information presented cause you to make any changes in how you do your job? ☐ Yes ☐ No
7. How committed are you to making these changes?
   (Not committed) 1 2 3 4 (Very committed)
8. Do you feel future activities on this subject matter are necessary and or important? ☐ Yes ☐ No

Follow-Up – As part of our ongoing quality-improvement effort, we would like to be able to contact you in the event we conduct a follow-up survey to assess the impact of our educational interventions on professional practice. Are you willing to participate in such a survey? ☐ Yes ☐ No

This lesson is a knowledge-based CE activity and is targeted to pharmacists and pharmacy technicians. This program has been approved for 1/2 contact hour of continuing education credit (0.05 CEU). To receive continuing education credit, please provide the following information:

Circle correct test answers and return to:
NEW JERSEY PHARMACIST ASSOCIATION
Attention: **Journal C.E. Department, 760 Alexander Rd., PO Box 1, Princeton, NJ 08543-0001**
Enclosed is my check for: ☐ NJPhA Member **(FREE)** ☐ $15.00 Non-member
Statements of Credit will be uploaded to www.mycpemonitor.net
Name _____
Address _____
City _____ State_____ Zip _____
Email _____
Phone Number_____ License No._____
E-PID#_____ Birth mm/dd_____

2014 Convention Poster Presentations

The following are the posters presented at the New Jersey Pharmacists Association 2014 Convention in Asbury Park, NJ, September 19-21, 2014. The non-peer reviewed abstracts indicate original presentations. The subsequent list indicates encore presentations.

Drug Pricing Estimations with Smartphone Applications.

Sebastian Choi, PharmD Candidate, Hayeon Na, PharmD. Candidate
St. John's University College of Pharmacy & Health Sciences, Queens, NY.

Objective: To compare the drug-pricing smartphone applications that are currently available for the consumers in the New York City area.

Background: Despite the measures being taken to provide health insurance to off-set drug costs, many consumers still remain uninsured or underinsured. With the increasing accessibility of advanced technology, consumers have the ability to estimate out-of-pocket drug costs using web-based resources including smartphone applications. Smartphone applications have the ability to determine or estimate out-of-pocket drug costs based on the medication, the pharmacy, and the location. However, these smartphone applications may vary greatly in their responses, even when the same data is entered. These discrepancies may result in an inconsistent and unpredictable drug procurement experience for the patients.

Methods: A list of smartphone applications was formulated using search term "drug pricing applications" in the Google search engine. Each application was found and downloaded through Apple's iTunes and Google Play Store in July 2014. Smartphone applications were included if they were capable of providing an estimated out-of-pocket drug cost. Smartphone applications were excluded if they were non-functional or did not provide an estimated out-of-pocket drug cost. We selected the top ten medications based on prescription sales from the list of the "Top 200 Drugs" for the 2013 fiscal year (January to December 2013). These agents were chosen to test the extent of the smartphone applications' pricing functions. Zip codes from the middle of each of the five boroughs in New York City were used to eliminate location bias and for comparison (i.e.: 10036, 10314, 10460, 11226, 11367). The three applications were also compared in their methods of presentation and ease of navigation. The appropriate statistical analysis will be conducted to measure the degree of correlation.

Results: pending

Conclusion: pending

A Study to Determine the Types of Phosphate Binder Medications used in ESKD Patients.

Timothy Nguyen, PharmD, BCPS, Tommy Hyunh, Trung Pham.

Purpose: Chronic Kidney Disease (CKD) is a complex disease and one of its common complications is associated with hyperphosphatemia. This can lead to the development of severe hyperparathyroidism, soft tissue calcification, calcification of the lung, morbidity and mortality. The mainstream therapy for managing hyperphosphatemia is phosphate binders, vitamin D, cinacalcet and dialysis. There are multiple phosphate binder medications (PBM) available. The purpose of this research is to determine the types of PBM used in ESKD patient.

Methods: Retrospective data analysis of 150 ESKD patients during the spring of 2014. Data includes demographic information and the types of PBM patients were receiving. The types of PBM were grouped into non-calcium based (e.g., sevelamer), calcium-based, or both, or those did not take any PBMs. The data were tracked on the Excel Spreadsheet and the results were analyzed using simple descriptive statistics.

Results: Sevelamer was the most commonly used PBM (42%), and calcium acetate was the second most commonly used PBM (29%), combination therapy (11%), and those were not on any PBMs or were on hold at the time of the data collection (18%).
Conclusion: Hyperphosphatemia is a common condition in ESKD patients. Managing and controlling phosphate levels are important in reducing the overall morbidity and mortality. The most common types of phosphate binder medications used in ESKD patients were sevelamer and calcium acetate.

Incorporating Team-based Learning into a Physician Assistant Clinical Pharmacology Course.

Timothy Nguyen, PharmD, BCPS; Elaine Wong, PharmD, BCPS; Antony Pham, PharmD, BCPS.

Objective: To describe and compare the effectiveness of team-based learning (TBL) to that of traditional lectures in a Clinical Pharmacology course taught in the Physician Assistant program at Long Island University.

Design: Clinical Pharmacology Course taught in the Physician Assistant Program recently incorporated TBL activities and approximately fifty percent of the curriculum was delivered using a TBL format. Thirty-three students completed a pre- and post-survey, at the beginning of the first class and at the end of the last class, respectively. The evaluations and exam results were compared with outcomes from the previous year that were taught using traditional lecture styles.

Assessment: Pre- and post-surveys demonstrated mixed responses on TBL versus traditional lecture styles. In comparing student performance on exams from the previous year, outcomes were similar.

Conclusion: Incorporating TBL into the Physician Assistant clinical pharmacology course at Long Island University produced similar exam results compared to traditional lecture styles from the previous year. However, students expressed mixed responses regarding the TBL approach.

Cost Savings from Consultant Pharmacist Intervention in Antipsychotic Reduction in the Long-term Care Setting.

Douglas Wessel, RPh, PharmD, CCP; Nicole Skyer-Brandwene, RPh, MS, BCPS, CCP; Ryan Lu, PharmD Candidate.
Pharmacare, Inc, Clark, NJ.

Introduction: In an effort to reduce the inappropriate use of antipsychotics in the long-term care setting, pharmacy consultant have been utilized by expanding their role. Consultant pharmacists dedicated time in certain facilities to coordinate with the interdisciplinary team, search for creative non-drug interventions, and perform data collection.

Objective: The goal was to discontinue and/or reduce doses of unnecessary antipsychotic medications, increase quality of life for patients, and demonstrate effectiveness of consultant pharmacists in leading interdisciplinary teams. In doing so, significant medication cost savings could potentially be realized.

Methods: Four consultant pharmacists in six facilities participated in the project. The pharmacists coordinated with multiple disciplines within these facilities to identify a total of 185 residents on antipsychotics. The requirements of these participating patients were that they were on at least one antipsychotic, were covered by Medicare and were long stay patients. Patients were removed from the project if they were discharged from the facility or expired. Additional patients were added throughout the project to keep the total number in the group stable. Facilities were visited at least monthly for up to 20 months and antipsychotic data was collected monthly through a Google® spreadsheet. During the project, multiple antipsychotic doses were reduced and discontinued. Medication cost savings were estimated by using the average wholesale price of standard daily doses of the antipsychotics that were discontinued. The cost of consultant pharmacists' time in facilities was also estimated. The total estimated cost savings = (medication cost savings)-(cost of consultant pharmacist).

Results: Over the 2 year project, 46% of antipsychotics were discontinued, which can lead to significant medication cost savings and other healthcare cost savings such as reduced nursing time administering medications and reduced adverse drug events. Facilities saw an estimated total cost savings of $34,000-$46,000 per year. If this project was expanded to all of the long-term care facilities in New Jersey, the potential total savings would be projected at $12-$16 million per year.

Conclusion: This project shows that the consultant pharmacist, working with a multidisciplinary team, is effective in reducing unnecessary antipsychotic drugs and achieving cost-savings in the long-term care setting. The cost of the consultant pharmacists' time is a small fraction of potential medication dollars that can be saved.

Encore posters:

Evaluation of the Incorporation of a Commercially Available Simulated Electronic Medical Record (SimEMR) in a Simulated Introductory Pharmacy Practice Experience (IPPE).

Maria Leibfried, BS, PharmD, BCNSP, CCP; Michele Pisano, PharmD, CGP.
St. John's University College of Pharmacy & Health Sciences, Queens, NY.

Originally presented at American Association of Colleges of Pharmacy (AACP) Annual Meeting 2014, Grapevine, TX (July 26-30, 2014).

Influence of Pharmacy Consultants on Inappropriate Use of Antipsychotic Medications in Long-Term Care Facilities as Part of a Multidisciplinary Quality Improvement Project.

Nicole Skyer-Brandwene, RPh, MS, BCPS.
Healthcare Quality Strategies, Inc., Marlboro, NJ.

Originally presented at American College of Clinical Pharmacy Annual Virtual Poster Symposium, May 21, 2014. Pharmacotherapy June 9, 2014;34(6):e98.

New Scholarship Fund at PCP

Philadelphia College of Pharmacy (PCP) at University of the Sciences has established a scholarship in honor of past NJPhA president: Tom Bernhardt. Before joining the PCP faculty in 1978, Tom was the CE coordinator for NJPhA organizing the delivery of CE programs throughout New Jersey. Tom was a loyal NJPhA member, serving as president from 1989 to 1990. As a PCP faculty member, Tom coordinated and developed PCP's clerkship programs; he impacted students for more than 30 years.

PCP scholarships are fundamental for current students as they endeavor to afford their pharmacy training. The Tom Bernhardt Scholarship will be awarded to a pharmacy student in their final professional year, who has a minimum GPA of 3.0, and who exhibits excellence in experiential rotations. Tom was a dedicated NJPhA member and beloved PCP faculty member; please join us in commemorating Tom by making a gift to the Tom Bernhardt Scholarship fund today!

Give Online: www.usciences.edu/giveonline (Gift Designation—Other—Tom Bernhardt Scholarship Fund).

Please send checks to:

Office of Institutional Advancement, Box 54
University of the Sciences
600 S. 43rd Street,
Philadelphia, PA 19104

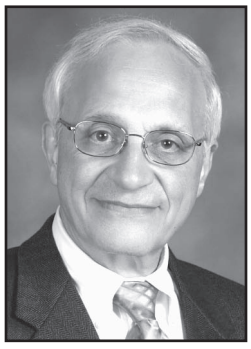
Congratulations to Our 2014 Award Recipients

One of the most gratifying events during an Annual Convention is the Awards Presentation. It is an opportunity to recognize, thank, and celebrate the incredible accomplishments of our members. Our roster of recipients in 2014 shows just how much talent and dedication there is among pharmacists. Congratulations to all our recipients.

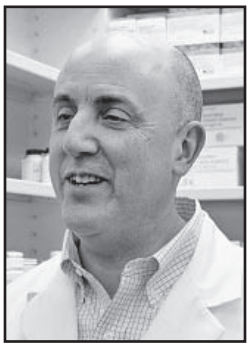
Congressman Frank Pallone, Jr.
Recipient of the Mortar and Pestle Award

Maria Troncone Leibfried, BS, PharmD, BCNSP, CCP
recipient of the Bowl of Hygeia Award

Ivan Saiff, RPh
Recipient of the Rosario "Russ" Mannino Pharmacist of the Year Award



John L. Colaizzi, Sr., PhD, RPh
Recipient of the Frederick B. Kilmer Award

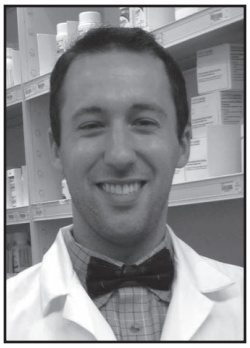


James P. Cammarata, RPh
Recipient of the NASPA Excellence in Innovation Award

Ritesh Shah, RPh
Recipient of the Andrew J. Preston PAC Award

Moriah Weissman, PharmD, CCP
Recipient of the NCPA Pharmacy Leadership Award & the Pharmaceutical Industry Award

Timothy Nguyen, PharmD, BCPS
Recipient of the Donald J. Wernik Academic Achievement Award



Brian J. Catton, PharmD
Recipient of the Pharmacists Mutual Distinguished Young Pharmacist Award

Mark K. Taylor, RPh, FACVP
Recipient of the Buy SellaPharmacy.com Independent Pharmacist of the Year Award

Ruth A. Marietta, RPh, CCP
Recipient of the Cardinal Health Generation Rx Champions Award

Ronald J. Mannino, RPh
Recipient of a Presidential Citation

Practice Spotlight:

On June 30, 2014, The Valley Hospital in Ridgewood, NJ, honored pharmacist Adedolapo (Dolly) Ademodi-Gbogodo with the Cognitive Clinical Talent Award for Clinical Excellence. This recognition of clinical excellence is bestowed for documenting 29,015 clinical interventions in 2013. This is the fourth year in a row that Dr. Ademodi-Gbogodo has earned this award. Overall, pharmacists at The Valley Hospital documented an impressive 189,334 clinical interventions in 2013. The hospital ceremony offered well-deserved congratulations to all of the Pharmacy Department.

The Valley Hospital is a fully accredited, acute care, not-for-profit hospital serving more than 440,000 people in 32 towns in Bergen County and adjoining communities. Valley serves the community by providing thousands of hours of healthcare education and screenings, support groups and classes to assist those in need, and care to all those who come through its doors, regardless of their ability to pay, as part of its commitment to giving back to the community.

Pharmacist receives Cognitive Clinical Talent Award for Clinical Excellence

Depicted in the picture (left to right) are: Richard Keenan, Chief Financial Officer, Valley Health System; Julie Karcher, Vice President VH Administration; Adedolapo (Dolly) Gbogodo, PharmD, award recipient; Ronald Krych, Director of Pharmacy

Region News

REGION 5 NEWS

By Alan "Scoop" Aronovitz, RPh, C.C.P.
NJPhA Region 5 - Second Vice President and Secretary

Congratulations to Heather Fascia, NJPhA student member and daughter of Region 5 member David Fascia, who graduated from Palm Beach Atlantic University Gregory School of Pharmacy on May 9th, 2014, with a Doctorate of Pharmacy degree. Heather is a member of the Pharmacy fraternity Phi Delta Chi and the Christian Pharmacist Fellowship International (CPFI).

Congratulations are also in order for Region 5 Treasurer and Trustee Mark Taylor, whose Jersey Shore Pharmacy in Egg Harbor Township is now accredited by the Pharmacy Compounding Accreditation Board (PCAB) for sterile and non-sterile compounding. PCAB accreditation gives patients, prescribers, and payers a way to select a pharmacy that meets or exceeds USP's high quality standards. Mark stated, "We are one of 8 pharmacies in New Jersey that are PCAB accredited. Our pharmacists and technicians worked extremely hard to get this accreditation and we will continue to provide quality compounded products to our customers."

The first annual Frank and Rachel Zammarelli Lecture took place at the Temple University School of Pharmacy in February of 2014. The Frank and Rachael Zammarelli Lecture Fund was established in 2011 by Amelia Z. Batastini, PHM '59, to provide an endowment for an annual lecture at the School of Pharmacy, in loving memory of her parents.

The first annual Paul and Amelia Batastini Lecture at the Temple University School of Dentistry took place on May 7, 2014. Paul Batastini Jr., *DEN '60,* met his future wife, Amelia Zammarelli, *PHR '59,* at a fraternity party while they were Temple students. They married three years later, in 1959 and have five children who became pharmacists, lawyers, and orthodontists. All of them are Temple alumni.

Congratulations to Caroline Vizzi, daughter of Lyn Batastini Vizzi and granddaughter of Amelia Batastini, who will attend the Temple University School of Pharmacy in the fall of 2014. Lyn is also pleased to announce her other daughter, Rachael Vizzi's new position as Executive Scientific Assistant at the American Association for Cancer Research.

Congratulations to Jillian H. Aronovitz, daughter of Region 5 Second Vice-President and Secretary Alan S. Aronovitz, who graduated from New York University on May 19th, earning a master's degree in mental health and wellness counseling. Upon graduation, Jillian began her new position as an Eating Disorders Counselor at the Renfrew Center in Boston, MA. Renfrew is the first and largest eating disorder treatment network in the country.

In an effort to become involved in community and medical groups in all the counties that make up our region, Region 5 has joined the Cumberland County Healthy Communities Coalition (CCHCC). The CCHCC is committed to reducing substance abuse among youth and strengthening the community through prevention education and collaboration. The Coalition is comprised of key stakeholders from the entire community that including representatives of youth, educators, law enforcement, parents, faith leaders, health professionals, media, local government, and business.

This endeavor resulted in an invitation to the Cumberland County Prescription Drug Abuse and Heroin Conference, held at the Cumberland County College in Vineland, NJ. on May 7th. The Cumberland County Prosecutor's Office, the CCHCC, and the SCRATCH Coalition hosted a conference for professionals to discuss the realities surrounding prescription drug abuse and heroin that are currently threatening the lives and well-being of our community. We were asked to provide a panelist for the conference and Joseph A. Barone, Dean of the Rutgers Ernest Mario School of Pharmacy recommended faculty member, Lucio Volino, Clinical Assistant Professor in the Department of Pharmacy Practice and Administration. During the panel discussion, Dr. Volino spoke about the part pharmacists play in preventing drug diversion, the value of using the NJ Prescription Monitoring Program (PMP), and the importance of communicating with all healthcare stakeholders. His points were very well received and even elicited praise for the role pharmacists on the healthcare team from the physician on the panel.

Alan S. Aronovitz has been representing us at the CCHCC monthly meetings but we are looking for others who would also like to attend. Please contact Alan at ASAXPCS@aol.com if you are interested.

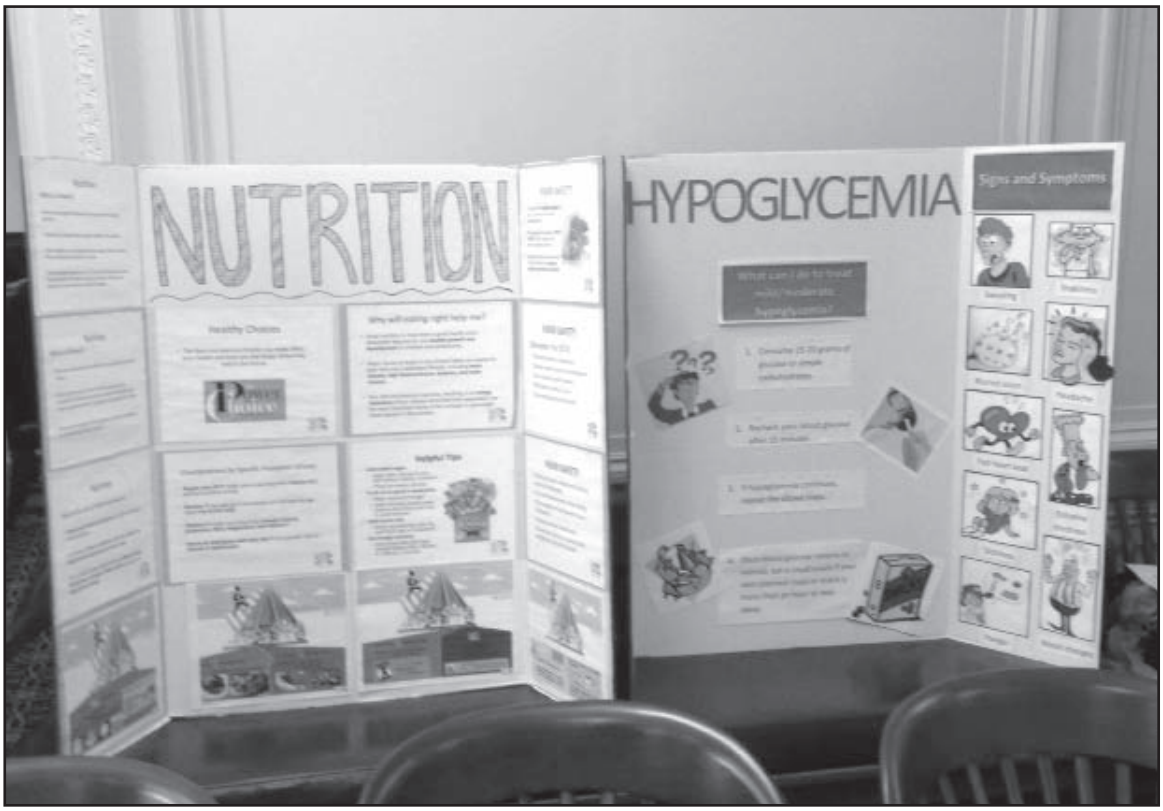
The next day, May 8th, Alan traveled to Washington, DC to meet with our NJ legislators as part of the NCPA Legislative Conference. With outstanding leadership provided by Elise Barry and Laurie Clark, the NJ delegation spent the day impressing on our representatives the importance of pharmacists to the communities they serve and the need for their support of the legislative issues we brought to their attention. All members are urged to contact their federal representatives and ask for their support to pass HR 4577, HR 4437, HR4190, and S867.

On February 26th, Region 5 hosted a continuing education program on Medication Safety presented by Steven L. Sheaffer, Pharm. D., of the University of the Sciences Philadelphia College of Pharmacy. Our second program, on May 21st, Addiction-Choice vs. Chronic Disease was presented by George Downes, Pharm. D., also of the University of the Sciences Philadelphia College of Pharmacy. We'd like to thank both presenters for their exceptional and informative lectures. Please monitor your e-mail for our next CE Dinner program, "Drug-Induced Photosensitivity & Lyme Disease" to be held on August 13, 2014.

Region 5 is seeking nominations for Second Vice-President and Treasurer for the 2014 – 2015 term. We are also seeking members interested in serving on our Regional Board of Directors (RBOD), these include Secretary, County Directors - one representative from each county, and our Committee Chairpersons. Our Committees include continuing education, finance, awards and scholarships, membership, public health and relations, permanent organization, students, and technicians. If you are interested in serving please send an e-mail to ASAXPCS@aol.com.

Student Day in Trenton on October 16, 2014

Students performed health screening and blood pressure readings for legislators, legislative staff and the public. They also discussed their educational posters.



Provided by the Ohio Pharmacists Foundation

continuing education for pharmacists

Volume XXXII, No. 3

Acute Bacterial Skin and Skin Structure Infections: Review and Update

Mona T. Thompson, R.Ph., PharmD

Mona T. Thompson has no relevant financial relationships to disclose.

Goal. The goal of this lesson is to provide a review of and update for the treatment of select acute bacterial skin and skin structure infections that are commonly seen and treated in the community. This lesson reviews treatment recommendations published by the Infectious Disease Society of America (IDSA), and antimicrobials with methicillin-resistant *Staphylococcus aureus* (MRSA) activity.

Objectives. At the completion of this activity, the participant will be able to:

1. recognize the different types of skin and skin structure infections discussed in this lesson;
2. demonstrate an understanding of the emergence of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) in acute bacterial skin and skin structure infection;
3. identify empiric antimicrobial treatment options for impetigo, erysipelas, nonpurulent, and purulent cellulitis; and
4. list fundamental prescribing and patient counseling points for the entities discussed.

Introduction

Acute bacterial skin and skin structure infections (ABSSSI), previously referred to as uncomplicated and complicated skin and skin structure infections (SSTI), present as a wide spectrum of disease. Disease may range from mild to severe, and includes impetigo, abscess, erysipelas, cellulitis, necrotizing fasciitis, and other soft tissue infections. Soft tissue refers to tissues that connect, support, or surround other structures and organs of the body that are not bone. Examples of soft tissue include muscle, tendons, fat, and blood vessels. The mechanism of such infections varies and may result secondary to minor or major abrasions, wounds, trauma, animal or human bites, or surgical site infections, among others.

ABSSSI are typically caused by gram-positive pathogens, including *Staphylococcus aureus* (*S. aureus*) and β-hemolytic streptococci. However certain gram-negative and anaerobic bacteria are also found in polymicrobial infections. Over the past decade, widespread emergence of community-associated [also referred to as *acquired*] methicillin-resistant *S. aureus* (CA-MRSA) has been reported. Previously, MRSA infections were limited to hospital-acquired infections or from other nosocomial sources.

While most uncomplicated SSTI can be successfully treated in the outpatient setting, complicated infections or those due to resistant organisms require intravenous treatment and/or hospitalization. Several newer intravenous antibiotics with MRSA coverage are available for the treatment of ABSSSI and include ceftaroline fosamil, daptomycin, linezolid, and telavancin. Outpatient parenteral antimicrobial therapy (OPAT) may be an option in select patients to prevent or shorten hospitalizations, decrease readmission rates, and reduce nosocomial infections and complications. Complicated skin and skin structure infections are one of the most common infections treated with parenteral antibiotics outside of the hospital.

The major types of skin and soft tissue infections that will be discussed in this lesson include impetigo, abscess, cellulitis, and erysipelas. With the exception of impetigo, treatment recommendations will be directed toward adults.

Impetigo

Impetigo is a contagious superficial bacterial skin infection commonly seen throughout the world. Its peak incidence is among children aged two to five years, but it can affect older children and adults. Impetigo occurs more frequently in tropical or subtropical climates, but is also prevalent in northern climates during the summer months.

Impetigo can occur as a result of either 1) bacterial invasion of previously normal skin, or 2) streptococcal colonization of intact skin followed by inoculation secondary to minor skin trauma, insect bites, etc. Risk factors include poverty, crowded living conditions, poor hygiene, and underlying scabies. Impetigo generally occurs on exposed parts of the body such as the face, especially around the nose and mouth, and on the arms

or legs. Handwashing remains an important measure in reducing the spread among children.

The disease presents as multiple localized lesions that are either non-bullous or bullous, ranging from the size of a dime to a quarter. With both forms, the lesions enlarge and progress from papules to vesicles and pustules. Over about one week, the lesions break down leaving a brown crust and possibly depigmented areas. Systemic symptoms are usually absent, but regional lymphadenitis may occur in non-bullous impetigo. Ecthyma is a more extreme and less common form of impetigo where the infection invades a deeper layer of the skin.

Impetigo is almost exclusively caused by *Staphylococcus aureus* and/or *β*-hemolytic streptococci (primarily Group A). Since the 1990s, *S. aureus* has emerged as the most common pathogen involved in impetigo (70 percent of cases). A smaller number of cases are also due to CA-MRSA. Bullous impetigo is caused by strains of *S. aureus* that produce a toxin causing cleavage in the superficial skin layer.

Group A streptococcus (GAS) that causes impetigo can also enter the respiratory tract resulting in strep throat. While impetigo and strep throat are mild illnesses due to GAS, "invasive GAS disease," which is severe and life threatening, can also occur when it enters other parts of the body such as blood, lungs, and muscle. Post-streptococcal glomerulonephritis and rheumatic fever following impetigo have also been described.

The goal of treatment includes relieving discomfort, improving cosmetic appearance of the lesions, preventing further spread of the infection both in the patient and to others, and preventing recurrence. Topical therapy is recommended over systemic therapy in cases where only a small number of non-bullous lesions are present.

Mupirocin 2 percent ointment (Bactroban®) has a labeled indication for impetigo, with directions to apply to the affected area three times a day. According to the IDSA 2011 MRSA infection treatment recommendations, mupirocin 2 percent ointment can be used in children with minor skin infections such as impetigo.

Fusidic acid cream is also effective, however, it is not available in the U.S.

A third topical agent, retapamulin (Altabax®), also carries an FDA-approved indication for children (nine months of age and older) and adults. This agent is the first member in a new class of antibacterial agents called pleuromutilins. Retapamulin only needs to be applied twice daily, compared to three times a day with mupirocin. However, it is more expensive and is not FDA-approved for the treatment of MRSA due to mixed results in clinical trials.

Advantages of topical therapy include delivery of high concentrations of drug to only infected tissue, minimization of systemic absorption and toxicity, and avoidance of altering gastrointestinal flora. The use of topical agents in limited impetigo may also minimize antibacterial resistance.

Oral antibiotics should be initiated in patients who do not tolerate a topical antibiotic, or in those with more extensive or systemic disease. The use of penicillin for primary treatment of GAS is no longer recommended. Since *S. aureus* now accounts for most cases, penicillinase-resistant penicillins or first-generation cephalosporins such as dicloxacillin, cephalexin, and amoxicillin/clavulanate are preferred. Clindamycin, an option for penicillin-allergic patients, is also appropriate. Macrolides are no longer adequate therapy due to resistant strains of *S. aureus* or *S. pyogenes*. Fluoroquinolones should also be excluded since MRSA resistance to this class is extensive. In communities with a high prevalance of CA-MRSA, agents such as clindamycin, trimethoprim-sulfamethoxazole (TMP-SMX), and tetracyclines may be used. Note that tetracyclines should not be used in children less than eight years of age. Duration of treatment is based on clinical improvement, while seven days is considered sufficient in most cases.

Abscess

An abscess is a collection of pus within the dermis or subcutaneous tissues. Patients will present with nodules and surrounding erythema. The presence of an abscess is significant as it differs from cellulitis, and is more likely to be due to *S. aureus*.

Abscesses are treated primarily by incision and drainage. Therefore, it is important that they are distinguished from cellulitis. Antibiotic therapy is recommended for abscesses when associated with severe or extensive disease (involving multiple sites of infection), or rapid progression along with cellulitis; signs and symptoms of systemic illness; comorbidities or immunosuppression; extremes of age; abscess in an area difficult to drain (face, hand, and genitals); septic phlebitis; and lack of response to incision and drainage alone.

Cellulitis and Erysipelas

Cellulitis and erysipelas are diffuse, acute, spreading infections of the dermis. These infections present with edema and redness, are warm to touch, and sometimes cause inflammation of the regional lymph nodes. Systemic symptoms are usually mild, but can include fever, tachycardia, confusion, hypotension, and leukocytosis.

While the terms *cellulitis* and *erysipelas* may be used interchangeably by physicians, there are distinguishing features. Erysipelas is a non-complicated form of cellulitis and is almost always a streptococcal infection (and occasionally *S. aureus*) that involves the superficial layers of the dermis. It is characterized by well-demarcated, raised areas of vivid erythema. Erysipelas is more common in infants, young children, and older adults, and more frequently affects the lower extremities. Prompt diagnosis and treatment corresponds

with a very good prognosis. The infection rarely extends into the deeper layers of the skin and soft tissues.

Alternately, cellulitis extends further into the deeper dermis and subcutaneous tissue and has less defined margins. Cellulitis is either purulent or nonpurulent. Purulent cellulitis is defined as cellulitis with associated purulent drainage or exudate in the absence of a drainable abscess.

Cellulitis and erysipelas result when organisms enter through breaches in the skin, most often on the lower legs. Other common sites include the upper extremities, trunk, perineum, or head and neck. Predisposing factors for these infections include conditions that make the skin more fragile or make local host defenses weaker. Examples include obesity, previous cutaneous damage, edema from venous insufficiency or lymphatic obstruction, and prior radiation therapy. The break in skin may be due to trauma, pre-existing skin infections such as impetigo, ulceration, or eczema among others. The breaks can be so small that they are not clinically apparent. Surgical procedures that disrupt lymphatic drainage (e.g., axillary node dissection for breast cancer) increase the risk of cellulitis.

Blood culture results are positive in fewer than 5 percent of cases. Other potential sources for culture include peripheral blood, needle aspirates, and skin biopsies. Surgical specimens in cases with purulence, abscess, or necrosis may be cultured, but many cases are nonpurulent.

Traditionally, cellulitis and erysipelas were managed empirically with agents that covered β-hemolytic streptococci and methicillin-sensitive *S. aureus* (MSSA). For classic erysipelas, penicillin has remained first-line therapy. However, because these two infections can be difficult to distinguish, they are often treated the same.

In 2005, IDSA released guidelines for SSTI, listing the following antibacterials as suitable agents for empiric outpatient treatment: dicloxacillin, cephalexin, or clindamycin. Treatment may also need to be directed to other organisms including gram-negative organisms which can produce cellulitis in certain circumstances. Table 1 lists risk factors for other pathogens that may be involved in cellulitis. At the time of preparing the 2005 guidelines, IDSA did not recognize the role of CA-MRSA in cellulitis and, therefore, did not recommend empiric coverage. However, in 2011, IDSA published their first guideline specifically for the treatment of MRSA with recommendations on the management of some of the most common clinical syndromes encountered including skin and skin structure infections. These two guideline documents are the basis of the recommendations in this lesson.

Table 1
Risk factors for associated pathogens in cellulitis*

Reported risk factors for MRSA
- Previous history of hospitalization or surgery within the past year
- Residence in a long term care facility within the past year
- Hemodialysis
- Previous MRSA infection or colonization
- Recent antibiotic use
- Contact sports
- Patient report of "spider bite"
- Purulent soft tissue infections
- Crowded living environments, such as homeless shelters, prisons, etc.
- Intravenous drug use
- Men who have sex with men
- Household contacts with MRSA infection

Risk factors associated with other pathogens

Diabetic foot infections	Often polymicrobial, including gram-positive and gram-negative aerobes and anaerobes
Neutropenia	Gram-positive, gram-negative including *Pseudomonas aeruginosa*
Intravenous drug use	*Staphylococcus aureus*, *Pseudomonas aeruginosa*
Human bites	Polymicrobial mixture of oral anaerobes and aerobes
Dog and cat bites	Polymicrobial mixture of pathogens derived from the animal and host skin flora

* Derived from retrospective studies; may not discriminate between MRSA and non-MRSA infections. Adapted from *Am J Med.* 2011;124(12).p1116.

Increasing Prevalence of CA-MRSA

The prevalence of CA-MRSA has increased in the last decade and is currently a prominent cause of purulent ABSSSI in the United States. Data from a Los Angeles emergency department (ED) indicated that infections from CA-MRSA more than doubled within a five-year period in patients presenting with purulent ABSSSI, from 29 percent in 2001 to 64 percent in 2005.

CA-MRSA strains are more virulent than health care-associated (HA-MRSA) strains and may carry genes that involve toxins associated with tissue necrosis and more serious disease. CA-MRSA skin infections range from cutaneous abscesses to necrotizing fasciitis. CA-MRSA can also cause severe systemic infections including pneumonia and bloodstream infections. Unlike HA-MRSA, many CA-MRSA strains are susceptible to gentamicin, tetracyclines, lincosamides, and TMP-SMX. CA-MRSA refers to MRSA infections that occur in outpatients or within 48 hours of hospitalization, and lack nosocomial exposures such as indwelling device, recent hospitalization, surgery, dialysis, or residence

Table 2
Recommended antimicrobial therapy for patients with cellulitis

	Antimicrobial	Dose
Outpatient purulent cellulitis	Clindamycin	300-450 mg PO TID
	TMP-SMX	1-2 DS tab PO BID
Treatment for CA-MRSA	Doxycycline	100 mg PO BID
	Minocycline	200 mg x 1, then 100 mg PO BID
	Linezolid	600 mg PO BID
Outpatient nonpurulent cellulitis		
Treatment for streptococci and MSSA	Cephalexin	500 mg PO QID
	Dicloxacillin	500 mg PO QID
Empiric coverage for CA-MRSA if no response or systemic toxicity	Clindamycin	300-450 mg PO TID
Hospitalized patients with cellulitis		
Treatment for MRSA	Vancomycin	15-20 mg/kg/dose IV every 8-12 hour
	Linezolid	600 mg PO/IV BID
	Daptomycin	4 mg/kg/dose IV QD
	Telavancin	10 mg/kg/dose IV QD
	Clindamycin	600 mg PO/IV TID
If nonpurulent cellulitis, may consider treatment for streptococci and MSSA with modification to MRSA-active therapy if no response	Nafcillin or Oxacillin	1-2 g IV every 4 hours
	Cefazolin	1 g IV every 8 hours

in a long-term care facility.

The IDSA document cites a study in which 73 percent of cases of nonpurulent cellulitis tested positive for serology to detect streptococci, indicating that it is still the predominant bacteria for nonpurulent cellulitis. On the other hand, a large study of purulent soft tissue infections in EDs across the U.S. found that 76 percent of cases were due to *S. aureus*, including 59 percent by CA-MRSA.

Hence, 2011 IDSA guidelines provide the following recommendations. 1) For outpatients with purulent cellulitis (e.g., cellulitis associated with purulent drainage or exudate in the absence of a drainable abscess), empiric therapy for CA-MRSA is recommended pending culture results. Listed options include clindamycin, TMP-SMX, a tetracycline (doxycycline or minocycline), and linezolid. Empiric therapy for infection due to β-hemolytic streptococci is likely to be unnecessary. 2) For outpatients with nonpurulent cellulitis (e.g., cellulitis with no purulent drainage or exudate and no associated abscess), empiric therapy for infection due to β-hemolytic streptococci is recommended. Listed options include cephalexin, dicloxacillin, and clindamycin. The role of CA-MRSA is unknown in nonpurulent cases, and empiric coverage for CA-MRSA is recommended only in patients who do not respond to β-lactam therapy or in those who are severely ill. If coverage for both CA-MRSA and β-hemolytic streptococci is needed, the clinician may prescribe clindamycin or linezolid alone, or TMP-SMX or a tetracycline plus a β-lactam such as amoxicillin.

Cultures are recommended in patients who have not responded adequately to initial treatment or if there is a concern for a cluster or an outbreak. Five to 10 days of therapy is recommended, but should be individualized based on the patient's clinical response for both types of cellulitis.

Patients with systemic toxicity and/or rapidly progressing or worsening infection despite receiving appropriate oral antibiotics may require inpatient management (i.e., intravenous antimicrobials) and surgical intervention. Hospitalized patients with complicated SSTI, defined as deeper soft tissue infections, surgical/traumatic wound infections, major abscesses, cellulitis, and infected ulcers and burns, should be treated with surgical debridement, broad spectrum antibiotics, and empiric therapy for MRSA pending culture results. Listed options include IV vancomycin, PO or IV linezolid, IV daptomycin, IV telavancin, and IV or PO clindamycin. A beta-lactam antibiotic, such as cefazolin or nafcillin, may be initiated in hospitalized patients with nonpurulent cellulitis and modified to MRSA therapy if there is no clinical response. Table 2 summarizes the recommended antimicrobial therapy for patients with cellulitis.

Recurrent MRSA SSTIs

Health care providers may instruct patients on measures to prevent recurrent MRSA infection such as keeping draining wounds covered with clean, dry bandages; maintaining good personal hygiene with regular bathing and handwashing with soap and water or alcohol-based hand gel; and avoiding the re-use or sharing of personal items that have contacted infected skin.

Experts define recurrent disease as two or more separate SSTI episodes at different sites over a six-month period. Environmental hygiene measures, with appropriate detergents or commercially available cleaners, may be used in patients with recurrent infections within a household or commu-

nity, and should be geared toward cleaning high-touch surfaces (i.e., surfaces that come into frequent contact with bare skin such as counters, doorknobs, bath tubs, and toilet seats).

Decolonization with mupirocin nasal and/or chlorhexidine topical antiseptic solution may be an option in patients who develop recurrent SSTI despite optimizing wound care and hygiene measures. While oral antimicrobial therapy for decolonization is not routinely recommended, it may be considered if infections recur regardless of measures. However, there are no published data to support the efficacy of decolonization in patients with recurrent MRSA SSTI. The optimal regimen, frequency of application, and duration of therapy are unclear.

Antimicrobials for the Treatment of CA-MRSA in SSTI

Trimethoprim-sulfamethoxazole (TMP-SMX), widely known by the trade names Bactrim™ or Septra®, is prescribed as one to two double-strength tablets orally twice daily for the treatment of MRSA in adults. This agent is not FDA-approved for the treatment of any staphylococcal infection; however, 95 to 100 percent of CA-MRSA strains are susceptible to it *in vitro* and it is an important option for outpatient management of SSTI. TMP-SMX is classified as pregnancy Category C/D, and is not recommended for women in the third trimester of pregnancy (or for children <2 months of age). Caution should be exercised when using this agent in the elderly, especially in those receiving concurrent inhibitors of the renin-angiotensin system and in those with chronic renal insufficiency because of an increased risk of hyperkalemia.

Oral tetracycline antibiotics that may be used for MRSA include doxycycline and minocycline. The adult dose for **doxycycline** is 100 mg orally twice daily. It is FDA-approved for the treatment of SSTI due to *S. aureus*, but not specifically for those caused by MRSA. For **minocycline**, a 200 mg oral loading dose is recommended, followed by 100 mg twice daily. These agents have *in vitro* activity and appear to be effective for this indication, but data are limited and lacking to support use in more invasive infections. **Tigecycline** (Tygacil®), a derivative of tetracycline, is an FDA-approved intravenous agent for the treatment of complicated SSTIs in adults. However, FDA recently issued a warning to consider alternative agents in patients with serious infections because of an increase in all-cause mortality. Tetracyclines are classified as pregnancy Category D, and are not recommended for children less than eight years of age because of the potential for tooth enamel discoloration and decreased bone growth.

Clindamycin, also an acceptable empiric treatment of purulent cellulitis, should be prescribed as 300 to 450 mg orally three times a day. Although not specifically FDA-approved for the treatment of MRSA infection, it has become widely used for the treatment of SSTI. The D zone test is recommended for detection of inducible clindamycin resistance in erythromycin-resistant, clindamycin-susceptible isolates, and is readily available. While *Clostridium difficile*-associated disease may occur with virtually any antibiotic, it may occur more frequently following clindamycin treatment when compared with other oral agents.

Linezolid (Zyvox®) is a gram-positive agent that is bacteriostatic against enterococci and staphylococci, and bactericidal against most strains of streptococci. It is of the oxazolidinone class, and exhibits its antimicrobial effect via inhibition of bacterial protein synthesis. Linezolid is active against problematic organisms such as MRSA, penicillin-resistant *Streptococcus pneumoniae*, and vancomycin-resistant enterococci (VRE). Resistance surveillance data indicates that more than 99 percent of *S. aureus* strains are susceptible to linezolid. It is FDA-approved for the treatment of complicated SSTIs and nosocomial pneumonia. The dosage is 600 mg orally or IV every 12 hours in children ≥12 years and adults. Linezolid does not require dosage adjustments in patients with either renal or hepatic impairment. It is rather expensive compared to other oral agents available for CA-MRSA.

Adverse effects were observed in some animal studies and there are no adequate, well-controlled studies in pregnant women. Therefore, this agent is classified as pregnancy Category C. Excretion in breastmilk is unknown, thus caution is advised.

Linezolid is contraindicated with concurrent use or within two weeks of MAO inhibitors; and in patients with uncontrolled hypertension, pheochromocytoma, thyrotoxicosis, and/or those taking sympathomimetics, vasopressive agents, and dopaminergic agents unless closely monitored for increased blood pressure. Additionally, linezolid should not be administered to patients taking SSRIs, tricyclic antidepressants, serotonin 5-HT1 receptor agonists (triptans), meperidine or buspirone, unless closely monitored for signs or symptoms of serotonin syndrome.

Tyramine, an amino acid that helps regulate blood pressure, is naturally occurring in the body and is found in certain foods. Ingestion of foods rich in tyramine such as aged cheeses, cured meats, fermented cabbage, soy sauce, or broad bean pods, such as fava beans, should be avoided as this can cause sudden and severe high blood pressure. Food that has been improperly stored or spoiled can create an environment where tyramine concentrations may increase.

Thrombocytopenia has been reported with linezolid use and may limit its use in patients with pre-existing myelosuppression. Weekly CBC (complete blood count) monitoring is recommended, and the agent should be discontinued in circumstances where myelosuppression occurs or worsens. It has

also been associated with neuropathy and lactic acidosis. Other common adverse events include headache, diarrhea, insomnia, dizziness, rash, nausea, and vomiting.

Vancomycin is a glycopeptide that inhibits bacterial cell wall synthesis by blocking glycopeptide polymerization. While its use in ABSSSI does have some limitations, it is the most common choice for parenteral treatment of CA-MRSA with nearly 50 years of clinical use. Vancomycin is available in multiple generic formulations, reasonably well tolerated, associated with a low incidence of adverse effects, and is relatively inexpensive. Unfortunately, the susceptibility of MRSA to this antibiotic may be decreasing with increasing reports of clinical failure. The vancomycin breakpoints for susceptible, intermediate, and resistant minimum inhibitory concentrations (MIC) have been reduced in laboratory standards to reflect the changes that have been seen in MRSA vancomycin susceptibility. Studies have indicated that vancomycin tissue penetration is variable.

In 2009, the American Society of Health-System Pharmacists (ASHP), IDSA, and the Society of Infectious Diseases Pharmacists jointly issued a consensus statement on the therapeutic monitoring of vancomycin in adults. The panel agreed that antibiotics other than vancomyin should be considered when vancomycin MIC values are ≥2 mg/L because it is unlikely that effective serum concentrations will be achieved when keeping within therapeutic trough levels. The IDSA MRSA treatment guidelines note that, for most patients with SSTI who have normal renal function and are not obese, 1 gm IV every 12 hours is sufficient. It is recommended that trough serum vancomycin levels always be maintained above 10 mg/L to avoid development of resistance. Additionally, the panel recommends dosing vancomycin at 15 to 20 mg/kg/dose (based on actual body weight and not to exceed 2 gm/dose) every eight to 12 hours for seriously ill patients with MRSA infections and normal renal function. A loading dose of 25 to 30 mg/kg should also be considered in such instances. For these large doses, prolonging the infusion time to two hours, and using an antihistamine may reduce the risk of red man syndrome and possible anaphylaxis. For severe infections, higher trough concentrations of 15 to 20 mg/L are recommended to optimize pharmacodynamics, improve tissue penetration, and prevent resistance development. Serum trough concentrations should be obtained just prior to the fourth dose; monitoring of peak concentrations is not recommended.

Vancomycin has long been considered a nephrotoxic and ototoxic agent. Yet, according to the consensus statement, there are limited data suggesting a direct causal relationship between toxicity and specific serum vancomycin concentrations. In summary, trough monitoring is best suited for patients receiving aggressive dosing, those receiving concurrent nephrotoxins, patients with unstable renal function, or those receiving prolonged courses of therapy. There are limited data to support the safety of sustained trough serum vancomycin concentrations of 15 to 20 mg/L.

Daptomycin (Cubicin®) is a lipopeptide class antibiotic that disrupts cell membrane function via calcium-dependent binding, resulting in bactericidal activity in a concentration dependent manner. It is FDA-approved for adults with SSTI due to *S. aureu*s among other indications. The dose is 4 mg/kg of total body weight once daily IV for seven to 14 days. The frequency of administration should be reduced to every 48 hours in patients with CrCl <30mL/min. Elevations in creatine phosphokinase (CPK), which are rarely treatment-limiting, have occurred in patients receiving higher doses such as 6 mg/kg for other indications. Patients should be monitored, however, for signs and symptoms of infection with suggested CPK weekly monitoring during therapy. The label recommends more frequent monitoring with current or previous statin therapy, unexplained CPK increases, or renal impairment. Daptomycin may also cause false prolongation of the PT and increase of INR with certain reagents. This agent is classified as pregnancy Category B.

Ceftaroline (Teflaro®), the active form of ceftaroline fosamil, is a broad spectrum cephalosporin with potent activity against MRSA. It exerts bactericidal activity by binding to key penicillin binding proteins, with enhanced affinity to several resistant pathogens including MRSA and strains that vancomycin and daptomycin are ineffective against. However, unlike many other new agents discussed in this lesson, ceftaroline is active against common gram-negative and some anaerobic bacteria. For complicated SSTI, the dose is 600 mg IV every 12 hours. Renal dosage adjustments are required for CrCl <50 mL/min. It is the only β-lactam with activity against MRSA.

Telavancin (Vibativ®) is an intravenous lipoglycopeptide that inhibits cell wall synthesis leading to cell membrane depolarization. This powerful agent is bactericidal against gram-positive pathogens including MRSA, as well as vancomycin-intermediate and vancomycin-resistant *S. aureus* (VISA, VRSA). It is FDA-approved for complicated SSTI in adults dosed at 10 mg/kg IV every 24 hours. It is classified as pregnancy Category C, as adverse developmental outcomes were observed in animal data. Telavancin may prolong the QT interval and should be avoided in patients with a history of QT prolongation or certain cardiac conditions. Caution should also be exercised in patients with renal impairment or in those receiving other nephrotoxic medications. In two clinical trials, nephrotoxicity was more commonly seen in patients treated with telavancin than among those treated with vancomycin. Although renal dysfunction seems reversible upon cessation of therapy, the manufacturer's label recommends monitoring renal

function during therapy and after discontinuation. The label also provides recommendations for dosage adjustments in patients with CrCl <50mL/min. Monitoring of serum levels is not available.

In December 2013, Cubist Pharmaceuticals announced that FDA had accepted the company's New Drug Application for its investigational antibiotic, tedizolid phosphate (PO and IV) with priority review. Cubist is seeking FDA approval of tedizolid for the treatment of ABSSSI. If approved, tedizolid will be the second oral FDA-approved antibiotic for the treatment of complicated SSTI caused by MRSA and an alternative to linezolid.

Conclusion

Skin and soft tissue infections are common across all ages. While generally caused by *S. aureus* and *β*-hemolytic streptococci, it is important to note the increasing prevalence of MRSA. Treatment options are expanding. For the most up to date information, refer to the IDSA guidelines.

The author, the Ohio Pharmacists Foundation and the Ohio Pharmacists Association disclaim any liability to you or your patients resulting from reliance solely upon the information contained herein. Bibliography for additional reading and inquiry is available upon request.

This lesson is a knowledge-based CE activity and is targeted to pharmacists in all practice settings.

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Acute Bacterial Skin and Skin Structure Infections: Review and Update CE exam on the following page

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Acute Bacterial Skin and Skin Structure Infections: Review and Update

1. Acute bacterial skin and skin structure infections are typically caused by:
   a. gram-positive pathogens. c. anaerobes.
   b. gram-negative pathogens.

2. Which of the following diseases presents as multiple localized non-bullous or bullous lesions?
   a. Abscess c. Erysipelas
   b. Cellulitis d. Impetigo

3. Since the 1990s, which pathogen has emerged as most commonly involved in impetigo?
   a. *S. pyogenes* c. CA-MRSA
   b. *S. aureus* d. Group A Streptococcus

4. An impetigo treatment option for penicillin-allergic patients is:
   a. cephalexin. c. dicloxacillin.
   b. clindamycin. d. fluoroquinolones.

5. Which of the following skin and skin structure infections (SSTIs) is described as a collection of pus within the dermis or subcutaneous tissue?
   a. Abscess c. Erysipelas
   b. Cellulitis d. Impetigo

6. Abscesses are primarily treated with antibiotics.
   a. True b. False

7. Cellulitis differs from erysipelas in that cellulitis:
   a. is almost always due to streptococci.
   b. involves the superficial layers of the dermis.
   c. is more common in infants and young children.
   d. extends into the deeper dermis and subcutaneous tissue.

Completely fill in the lettered box corresponding to your answer.

1.	[a]	[b]	[c]	6.	[a]	[b]	11.	[a]	[b]	[c]	[d]
2.	[a]	[b]	[c]	[d]	7.	[a]	[b]	[c]	[d]	12.	[a]	[b]	[c]	[d]
3.	[a]	[b]	[c]	[d]	8.	[a]	[b]	[c]	[d]	13.	[a]	[b]	[c]	
4.	[a]	[b]	[c]	[d]	9.	[a]	[b]			14.	[a]	[b]	[c]	[d]
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8. According to the 2011 IDSA guidelines, which of the following antimicrobials is considered a suitable agent for empiric outpatient treatment of purulent cellulitis?
   a. Dicloxacillin c. TMP/SMX
   b. Cephalexin d. Ciprofloxacin

9. Which MRSA strain is more virulent and may carry genes that involve toxins associated with tissue necrosis?
   a. CA-MRSA b. HA-MRSA

10. Published data support the efficacy of decolonization in patients with recurrent MRSA SSTI.
   a. True b. False

11. Trimethoprim-sulfamethoxazole should be used with caution in the elderly because of an increased risk of:
   a. hypertension. c. hypokalemia.
   b. hypotension. d. hyperkalemia.

12. Compared to other agents used to treat CA-MRSA, *Clostridium difficile*-associated disease may occur more frequently following treatment with:
   a. daptomycin. c. clindamycin.
   b. linezolid. d. doxycycline.

13. Which of the following agents is FDA-approved for treatment of complicated SSTIs and nosocomial pneumonia?
   a. TMP-SMX c. Linezolid
   b. Clindamycin

14. The susceptibility of MRSA to which of the following antibiotics may be decreasing with increasing reports of clinical failure?
   a. Vancomycin c. Daptomycin
   b. Linezolid d. Ceftaroline

15. Which of the following agents is active against common gram-negative and some anaerobic bacteria?
   a. Telavancin c. Daptomycin
   b. Vancomycin d. Ceftaroline

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New Drugs: Aptiom, Imbruvica, Luzu, and Sovaldi

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Dr. Thomas A. Gossel has no relevant financial relationships to disclose.

Goal. The goal of this lesson is to provide information on eslicarbazepine acetate (Aptiom®), ibrutinib (Imbruvica™), luliconazole (Luzu®) and sofosbuvir (Sovaldi™).

Objectives. At the completion of this activity, the participant will be able to:

1. recognize signs and symptoms, and key features of targeted pathologies including information on their prevalence;
2. recognize important therapeutic uses for the drugs and their applications in specified pathologies;
3. select the indication(s), pharmacologic action(s), clinical application(s), dosing regimens, route of administration, and availability of each drug;
4. demonstrate an understanding of adverse effects and toxicity, warnings, precautions, contraindications, and significant drug-drug interactions reported for each agent; and
5. list important counseling advice to convey to patients and/or their caregivers.

The four new-molecular entity drugs discussed in this lesson are indicated to treat a variety of pathologies (Table 1). This lesson provides a brief introduction to the drugs, and is not intended to extend beyond an overview of the topic. The reader is, therefore, urged to consult the products' full prescribing information leaflet (package insert), *Medication Guide* when available, and other published sources for detailed descriptions.

Eslicarbazepine Acetate (Aptiom)

Antiepileptic drugs (AED) are the major therapeutic intervention for epilepsy. A sizeable number of people with epilepsy experience pharmacoresistant seizures or encounter significant adverse effects with existing AED treatment. This poor response to seizure control means that combination therapy is recommended, but about 20 to 30 percent of patients continue to have seizures despite treatment with more than one AED. Therefore, there remains a need for new, effective AEDs, particularly those that can be used safely as adjuncts to standard therapy, to further reduce seizure frequency. Although structurally distinct from carbamazepine (e.g., Carbatrol, Tegretol) and oxcarbazepine (e.g., Trileptal, Oxtellar XR), eslicarbazepine acetate is chemically related to these carboxamide derivatives.

Indications and Use. Aptiom (ap-TEE-om) is indicated as adjunctive treatment of partial-onset seizures.

Partial-Onset Seizures. Epilepsy is caused by abnormal or excessive activity in the brain's nerve cells. Epilepsy is one of the most common neurological disorders and, according to the Centers for Disease Control and Prevention, affects nearly 2.2 million people in the United States, and up to 60 million people worldwide. Approximately 200,000 new cases of seizures and epilepsy occur in the United States each year. Partial-onset seizures are the most common type encountered in patients with epilepsy.

The International League Against Epilepsy classifies the disorder into three main types: partial (focal), generalized, and unclassified. Partial-onset epilepsy is restricted to discrete areas of the cerebral cortex while generalized epilepsy occurs in diffuse regions of the brain simultaneously. Because of the focused nature of a partial seizure, only a specific area of the body is usually involved. Treatment of partial-onset seizures is challenging since approximately 60 percent of patients with partial-onset seizures do not achieve seizure control with current AEDs.

Seizures can cause a wide range of symptoms, including repetitive limb movements, unusual behavior and generalized convulsions with loss of consciousness. Seizures can have serious consequences, including physical injury and death.

Mechanism of Action. Eslicarbazepine acetate is extensively converted to eslicarbazepine, which is considered to be responsible for therapeutic effects. The precise mechanism(s) by which eslicarbazepine exerts anticonvulsant activity is unknown, but is believed

Table 1
Selected new drugs

Generic (Proprietary) Name	Distributor	Indication	Dose*	Dosage Form*	Most Common Side Effects	Medication Guide±
Eslicarbazepine acetate (Aptiom)	Sunovion Pharmaceuticals Inc.	adjunctive treatment of partial-onset seizures	800 mg once daily	200, 400, 600, 800 mg tablets	(≥4%): dizziness, somnolence, nausea, headache, diplopia, vomiting, fatigue, vertigo, ataxia, blurred vision, tremor	Yes
Ibrutinib (Imbruvica)	Pharmacyclics	mantle cell lymphoma chronic lymphocytic leukemia	560 mg once daily 420 mg once daily	140 mg capsules	(≥20%): thrombocytopenia, diarrhea, anemia, neutropenia, fatigue, vomiting, nausea, musculoskeletal pain, upper respiratory tract infection, bruising, dyspnea, constipation, abdominal pain, decreased appetite, peripheral edema, rash	No
Luliconazole (Luzu)	Medicis (division of Valeant Pharmaceuticals)	interdigital tinea pedis tinea cruris tinea corporis	once daily for 2 weeks once daily for 1 week	1% topical cream	(<1%): application site reactions	No
Sofosbuvir (Sovaldi)	Gilead Sciences	chronic hepatitis C infection	400 mg once daily	400 mg tablets	(>20%): fatigue, headache§; fatigue, headache, nausea, insomnia, anemia#	No

*Recommended dose for most patients
±Availability at the time of publication of this lesson
§Sovaldi in combination with ribavirin
#Sovaldi in combination with ribavirin and peginterferon alfa

to involve inhibition of voltage-gated sodium channels in rapidly firing neurons. This may make it more effective in persons who have failed other sodium channel blockers due to developing pharmacoresistance to them.

Efficacy and Safety. Three clinical studies in which participants with partial-onset seizures were randomly assigned to receive eslicarbazepine acetate or placebo demonstrated that the drug is effective in reducing the frequency of seizures.

The most common adverse effects reported by patients receiving the drug in these clinical trials included dizziness, drowsiness, nausea, headache, double-vision, vomiting, fatigue and loss of coordination. Like other antiepileptic drugs, Aptiom may cause suicidal thoughts or actions in a very small number of patients.

Warnings, Precautions and Contraindications. The following **warnings** and **precautions** are listed:

• *Suicidal behavior and ideation*: Monitor for suicidal thoughts or behavior.

• *Serious dermatologic reactions:* Monitor for dermatologic reactions and discontinue in case of serious dermatologic reactions.

• *Drug reaction with eosinophilia and systemic symptoms*: Monitor for hypersensitivity. Discontinue if another cause cannot be established.

• *Anaphylactic reactions and angioedema*: Monitor for breathing difficulties or swelling. Discontinue the drug if another cause cannot be established.

• *Hyponatremia (sodium <125 mEq/L)*: Monitor sodium levels in patients at risk or patients experiencing hyponatremia symptoms. Concurrent hypochloremia may also be present in patients with hyponatremia.

• *Neurological adverse reactions*: Monitor for dizziness, disturbance in gait and coordination, somnolence, fatigue, cognitive dysfunction, and visual changes. Use caution when driving or operating machinery.

• *Withdrawal of Aptiom*: As with all antiepileptic drugs, withdraw Aptiom gradually and avoid abrupt discontinuation to minimize the risk of increased seizure frequency and status epilepticus.

• *Drug-induced liver injury*: Discontinue Aptiom in patients with jaundice or evidence of significant liver injury.

• *Abnormal thyroid function tests*: Dose-dependent decreases in T3 and T4 have been observed. Evaluate for clinical signs and symptoms of hypothyroidism.

Hypersensitivity to eslicarbazepine acetate or oxcarbazepine is a **contraindication** to Aptiom.

Drug Interactions. Several considerations are listed:

•*Carbamazepine*: May need dose adjustment for Aptiom or carbamazepine.

•*Phenytoin*: Higher dosage of Aptiom may be necessary and dose adjustment may be needed for phenytoin based on clinical response and serum levels of phenytoin.

•*Phenobarbital or primidone*: Higher dosage of Aptiom may be necessary.

•*Hormonal contraceptives*: Aptiom may decrease the effectiveness of hormonal contraceptives. Females of reproductive potential should use additional or alternative non-hormonal birth control.

Administration, Dosing, and Availability. Start treatment at 400 mg once daily. After one week, increase dosage to 800 mg once daily, which is the recommended maintenance dose. Some patients may benefit from the maximum recommended maintenance dosage of 1200 mg once daily, although this dosage is associated with an increase in adverse reactions. A maximum dose of 1200 mg daily should only be initiated after the patient has tolerated 800 mg daily for at least a week. For some patients, treatment may be initiated at 800 mg once daily, if the need for additional seizure reduction outweighs an increased risk of adverse reactions during initiation. A dose reduction is recommended in patients with moderate and severe renal impairment (i.e., creatinine clearance <50 mL/min). Aptiom is marketed as tablets containing 200 mg, 400 mg, 600 mg, and 800 mg of eslicarbazepine acetate.

Patient Counseling Information. Specific points for patient counseling are summarized in Table 2.

Ibrutinib (Imbruvica)

Ibrutinib is the third drug approved to treat mantle cell lymphoma (MCL), following bortezomib (Velcade, 2006) and lenalidomide (Revlimid, 2013). FDA approved the drug under the agency's accelerated approval program. This permits FDA to approve a drug to treat a serious disease based on clinical trials showing that the drug has an effect on a surrogate endpoint, that is reasonably likely to predict a clinical benefit to patients. FDA granted orphan-product designation because it is intended to treat a rare disease.

Indications and Use. Imbruvica (im-BRU-vih-kuh) is indicated for treatment of patients with MCL who have received at least one prior therapy. This indication is based on overall response rate.

Imbruvica's indication was expanded in February of 2014 to include chronic lymphocytic leukemia (CLL). The dose for CLL is included in Table 1, but this indication will not be discussed further in this lesson.

Mantle Cell Lymphoma. MCL is a rare, aggressive form of non-Hodgkin lymphoma and represents about 6 percent of all non-Hodgkin lymphoma cases in the United States. Many secondary genetic events contribute to tumor growth in MCL, including the loss of DNA damage-response capacity, activation of cell-survival pathways, and inhibition of apoptosis (natural or programmed cell death). Prognosis in MCL is the worst among all B cell lymphomas. Historically, MCL has been treated like most other forms of B cell non-Hodgkin lymphoma, with regimens such as a combination of cyclophosphamide (e.g., Cytoxan), vincristine (e.g., Oncovin), doxorubicin (e.g., Adriamycin), and prednisone. However, early retrospective studies in the United States and Europe showed that MCL patients treated with such regimens had an overall survival of less than three years.

In the United States, 2,900 new cases of MCL are diagnosed each year with a median age at diagnosis of 65. By the time the cancer is diagnosed, it usually has already spread to the lymph nodes, bone marrow, gastrointestinal tract, spleen, and other organs.

Mechanism of Action. Ibrutinib is a small-molecule inhibitor of a cytoplasmic specific protein called Bruton's tyrosine kinase (BTK) expressed in B cells and myeloid cells. The drug forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK enzymatic activity. BTK is a signaling molecule of the B-cell antigen receptor and cytokine receptor pathways. BTK's role in signaling through the B-cell sur-

Table 2
Patient counseling information for Aptiom*

Inform patients:
•to read the FDA-approved *Medication Guide* prior to taking Aptiom and to re-read it each time the prescription is refilled, and to take the drug exactly as prescribed;
•that Aptiom may cause serious side effects including suicidal thoughts or behavior; potentially serious skin reactions including a rash, swelling of the face, eyes, lips, tongue, or difficulty in swallowing; liver disease; and neurological reactions including dizziness or vision problems, and to report any change from normal to their doctor at once;
•that the drug may lower their blood level of sodium and to report symptoms such as nausea, tiredness or lack of energy, irritability, confusion, muscle weakness/spasms, or more frequent or severe seizures to their doctor;
•that the drug may slow thinking or motor skills, so they should not drive or operate heavy machinery until they know how it affects them;
•to not stop taking their medicine without consulting their doctor;
•that female patients of childbearing age should use additional or alternative non-hormonal forms of contraception during treatment with Aptiom and for at least one month after treatment with Aptiom has been discontinued;
•to tell their doctor about all medicines they are taking. They should ask their pharmacist if they are not sure;
•to avoid giving Aptiom to other people even if they have similar symptoms. It may harm them.

*A complete list of information is available in the product's *Medication Guide*.

Table 3
Patient counseling information for Imbruvica*

Inform patients:
- to read the FDA-approved Patient Information leaflet;
- of the possibility of bleeding, and to report any signs or symptoms (blood in stools or urine, prolonged or uncontrolled bleeding). Tell them that Imbruvica may need to be interrupted for medical or dental procedures;
- of the possibility of serious infection, and to report any signs or symptoms (fever, chills) suggestive of infection;
- of the possibility of renal toxicity and advise them to maintain adequate hydration;
- that other malignancies have occurred in patients with MCL who have been treated with Imbruvica, including skin cancers and other carcinomas;
- of the potential hazard to a fetus and to avoid becoming pregnant;
- to take Imbruvica orally once daily according to their doctor's instructions and that the capsules should be swallowed whole, without being opened, broken, or chewed, with a glass of water at approximately the same time each day;
- that in the event of a missed daily dose of Imbruvica, it should be taken as soon as possible on the same day with a return to the normal schedule the following day, and that they should not take extra capsules to make up the missed dose;
- of the common side effects associated with Imbruvica;
- to inform their doctor of all medicines including prescription drugs and OTC products, vitamins, minerals, and herbal products they are taking;
- that they may experience loose stools or diarrhea, and to contact their doctor if diarrhea persists.

*A complete list of information is available in the product's Patient Information leaflet.

face receptors results in activation of pathways necessary for B-cell trafficking, chemotaxis, and adhesion. Ibrutinib inhibits malignant B-cell proliferation and survival.

Efficacy and Safety. Imbruvica's approval for MCL was based on a study with 111 participants who had received at least one therapy, and were given Imbruvica daily until their disease progressed or adverse effects became intolerable. Results revealed that nearly 66 percent of participants experienced tumor shrinkage or disappearance after treatment. An improvement in survival or disease-related symptoms has not been established.

The most common adverse effects reported for MCL were thrombocytopenia (low levels of platelets in the blood), diarrhea, neutropenia (decrease in infection-fighting white blood cells), anemia, fatigue, musculoskeletal pain, edema, upper respiratory infection, nausea, bruising, shortness of breath, constipation, rash, abdominal pain, vomiting, and decreased appetite. Other clinically significant adverse effects include bleeding, infections, kidney problems, and development of other types of cancers. The adverse reaction most frequently leading to treatment discontinuation with Imbruvica was subdural hematoma.

Warnings, Precautions and Contraindications. The following **warnings** and **precautions** are listed:

- *Hemorrhage*: Monitor for bleeding. The mechanism for bleeding events is not well understood.
- *Infections*: Monitor patients for fever and infections and evaluate promptly.
- *Myelosuppression*: Check complete blood counts monthly.
- *Serious and fatal renal toxicity*: Monitor renal function and maintain hydration.
- *Second primary malignancies*: Other malignancies have occurred in patients, including skin cancers, and other carcinomas.
- *Embryo-fetal toxicity*: Ibrutinib can cause fetal harm. Advise women of the potential risk to a fetus and to avoid pregnancy while taking the drug.

There are no **contraindications** listed.

Drug Interactions. Imbrutinib is primarily metabolized by cytochrome P450 enzyme 3A. Avoid co-administration with strong or moderate CYP3A inhibitors and consider alternative agents with less CYP3A inhibition. Concomitant use of strong CYP3A inhibitors taken chronically (e.g., ritonavir, indinavir, nelfinavir, saquinavir, boceprevir, telaprevir, nefazodone) is not recommended. For short-term use (seven days or less) of strong CYP3A inhibitors (e.g., antifungals and antibiotics), consider interrupting Imbruvica therapy until the CYP3A inhibitor is no longer needed.

Reduce Imbruvica dose to 140 mg if a moderate CYP3A inhibitor (e.g., fluconazole, darunavir, erythromycin, diltiazem, atazanavir, aprepitant, amprenavir, fosamprevir, crizotinib, imatinib, verapamil, grapefruit products, and ciprofloxacin) must be used.

Administration, Dosing, and Availability. Administer Imbruvica orally once daily, at approximately the same time each day. Swallow the capsules whole with water; do not open, break, or chew the capsules. The recommended dose for MCL is 560 mg orally once daily. If a dose of Imbruvica is not taken at the scheduled time, it can be taken as soon as possible on the same day, with a return to the normal schedule the following day. Extra capsules of the dose should not be taken to make up for the missed dose. The product is available as capsules containing 140 mg of ibrutinib.

Patient Counseling Information. Specific points for patient counseling are summarized in Table 3.

Luliconazole (Luzu)

Luzu (LOO-zoo) cream is the first topical azole antifungal approved to treat tinea cruris (jock itch) and tinea corporis (ringworm) with a one-week, once-daily treatment regimen. All other currently approved treatments require two weeks of treatment. For interdigital tinea pedis (athlete's foot between the toes), the treatment is once daily for two weeks. Luliconazole provides good efficacy and tolerability with a short duration of

treatment. The drug has been approved in Japan since 2005.

Indications and Use. Luzu cream is an azole antifungal indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum* and *Epidermophyton floccosum*, in patients 18 years of age and older.

Tinea Infections. Superficial mycoses (fungal) infections are not fatal, but they can seriously interfere with a patient's quality of life in view of the considerable discomfort such as itching and interference with sleep, and/or cosmetic deformity. These diseases are found worldwide and affect 20 to 25 percent of the world's population. Dermatophytosis (tinea infection) is the most common infection among the superficial mycoses. According to an epidemiological survey of ambulatory visits in the United States, the incidences of dermatophytosis were as high as 23.2 percent, 20.4 percent, and 18.8 percent respectively, during 1995 to 2004. *T. rubrum*, an anthropophilic (preferring humans to other animals) fungus, is the most prevalent causative agent of dermatophytosis in developed countries. Its incidence has not changed in recent decades, although many antifungal drugs with potent action against this species have become available during this period.

Mechanism of Action. Although the exact mechanism of action against dermatophytosis is unknown, luliconazole appears to inhibit fungal ergosterol synthesis by inhibiting the enzyme lanosterol demethylase. Inhibition of this enzyme's activity by azole antifungals results in decreased amounts of ergosterol, a constituent of fungal cell membranes, and a corresponding accumulation of lanosterol.

Efficacy and Safety. Approval was based on three pivotal U.S. trials that included 679 adults with either tinea pedis (two trials) or tinea cruris (one trial). For the two studies in tinea pedis with a treatment duration of two weeks, the primary endpoint was defined as complete clearance four weeks post-treatment. In study #1, 26 percent of participants treated with luliconazole were completely cleared, compared with 2 percent of those treated with vehicle alone. In study #2, 14 percent of participants treated with luliconazole were completely cleared, compared with 2 percent of those treated with vehicle alone. In the tinea cruris trial, complete clearance was assessed three weeks post-treatment. After one week of treatment, 21 percent of patients treated with luliconazole were completely cleared, compared with only 4 percent of those treated with vehicle alone.

The most common adverse events were mild application site reactions reported in less than 1 percent of subjects for both luliconazole and vehicle.

Warnings, Precautions and Contraindications. There are no **warnings**, **precautions** or **contraindications** listed.

Drug Interactions. The potential of luliconazole to inhibit cytochrome P450 enzymes (1A2, 2C9, 2C19, 2D6, and 3A4) was evaluated. When applied in therapeutic doses to patients with moderate to severe tinea cruris, luliconazole may inhibit the activity of CYP2C19 and CYP3A4. However, no *in vivo* trials have been conducted to assess the effect of luliconazole on other drugs that are substrates of CYP2C19 and CYP3A4. The drug is not expected to inhibit cytochromes 1A2, 2C9, or 2D6. The induction potential of luliconazole has not been evaluated.

Administration, Dosing, and Availability. When treating interdigital tinea pedis, a thin layer of Luzu cream should be applied to the affected skin areas and to about one inch of the surrounding healthy skin, once daily for two weeks. When treating tinea cruris or tinea corporis, Luzu cream should be applied in the same manner as tinea pedis above, once daily for one week. Luzu cream contains 1 percent luliconazole.

Patient Counseling Information. Specific points for patient counseling are summarized in Table 4.

Table 4
Patient counseling information for Luzu*

Inform patients:
- to read the FDA-approved Patient Information leaflet;
- that this medicine is for use on the skin only, and it should not be used on or near the eyes, mouth, or vagina;
- to tell the doctor if they are pregnant or plan to become pregnant, and about all medicines including prescription drugs and OTC products, vitamins, minerals, and herbal supplements they are taking;
- about possible side effects including skin irritation;
- to use the medicine exactly as the doctor instructs, and to wash their hands after applying Luzu cream.

*A complete list of information is available in the product's Patient Information leaflet.

Sofosbuvir (Sovaldi)

Sovaldi (soh-VAHL-dee) is the second drug approved by FDA during the last part of 2013 to treat chronic hepatitis C virus (HCV) infection. The other drug was simeprevir (Olysio).

Indications and Use. The drug is to be used as a component of a combination antiviral treatment regimen for chronic HCV infection. There are several different types of HCV infection. Depending on the type of HCV infection a person has, the treatment regimen could include Sovaldi and ribavirin (Copegus, Rebetol, & others) or Sovaldi, ribavirin, and peginterferon alfa (PEG-intron, Pegasys). Both ribavirin and peginterferon alfa are also used to treat HCV infection. If these other agents used in combination with Sovaldi are permanently discontinued, Sovaldi should also be discontinued. Sovaldi efficacy has been established in subjects with HCV genotype 1, 2, 3 or 4 infection, including those with hepatocellular carcinoma who are awaiting liver transplantation and those with HCV/HIV-1 co-infection.

Table 5
Patient counseling information for Sovaldi*

Inform patients:
- to read the FDA-approved Patient Information leaflet;
- that Sovaldi is used in combination with other antiviral medicines, and they should read the *Medication Guides* supplied with those other drugs. The drug should not be used alone;
- that Sovaldi may cause birth defects or death in an unborn baby, so the drug should not be used during pregnancy or if a female plans to become pregnant. Females and males must use two effective forms of birth control during treatment, and for six months after treatment with Sovaldi;
- to tell their doctor if they have liver problems or a liver transplant, kidney problems or if on dialysis, have HIV or any other medical conditions, or are breastfeeding or plan to breastfeed;
- to tell the doctor about all medicines including prescription drugs and OTC products, vitamins, minerals, and herbal supplements they are taking;
- to take Sovaldi exactly as the doctor prescribes, and to not stop taking it or change doses without telling their doctor;
- to tell the doctor about any side effect that is bothersome or does not go away;
- to keep Sovaldi in its original container and to not use if the seal over the bottle opening is broken or missing.

*A complete list of information is available in the product's Patient Information leaflet.

Before initiating treatment with Sovaldi, the following points should be considered: (1) monotherapy of Sovaldi is not recommended for treatment of chronic HCV; (2) treatment regimen and duration are dependent on both the viral genotype and patient population; and, (3) treatment response varies based on baseline host and viral factors.

Hepatitis C. As many as 170 million persons are chronically infected with HCV worldwide, with more than 350,000 dying annually from liver disease caused by HCV. Estimates of the number of persons in the United States who are chronically infected range from 2.7 million to 5.2 million. For previously untreated cases of HCV genotype 1 infection, representing more than 70 percent of all cases of chronic HCV infection in the United States, the current standard of care is 12 to 32 weeks of an oral protease inhibitor, combined with 24 to 48 weeks of peginterferon alfa plus ribavirin, with the duration of therapy guided by the on-treatment response and the stage of hepatic fibrosis. For patients infected with HCV genotype 2 or 3, until Sovaldi was approved, no direct-acting antiviral drugs had been available.

The virus causes inflammation of the liver that can lead to diminished liver function or failure. Most people infected with HCV are without symptoms of the disease until hepatic damage becomes apparent, which may take several years. Some people with chronic HCV infection develop scarring and poor liver function (cirrhosis) over many years, which can lead to complications such as bleeding, jaundice (yellowish eyes or skin), fluid accumulation in the abdomen, infections, or liver cancer.

Mechanism of Action. Sovaldi is a direct-acting antiviral agent against HCV. It is an inhibitor of HCV NS5B RNA-dependent RNA polymerase, which is essential for viral replication. Sofosbuvir is a nucleotide prodrug that undergoes intracellular metabolism to form the pharmacologically active uridine analog triphosphate, which can be incorporated into HCV RNA by the NS5B polymerase and acts as a chain terminator.

Efficacy and Safety. Effectiveness was evaluated in six clinical trials that consisted of 1,947 participants who had not previously received treatment for their disease (treatment-naïve) or had not responded to previous treatment (treatment-experienced), including participants co-infected with HCV and HIV. The trials were designed to measure whether HCV was no longer detected in the blood at least 12 weeks after finishing treatment (sustained treatment virologic response), suggesting a participant's HCV infection had been cured. Results from all clinical trials showed that a treatment regimen containing Sovaldi was effective in treating multiple types of HCV. Additionally, Sovaldi demonstrated efficacy in participants who could not tolerate or take an interferon-based treatment regimen, and in participants with liver cancer awaiting liver transplantation, addressing unmet medical needs in these populations.

The most common adverse effects reported in clinical study participants treated with Sovaldi and ribavirin were fatigue and headache. In participants treated with Sovaldi, ribavirin, and peginterferon alfa, the most common adverse affects reported were fatigue, headache, nausea, insomnia, and anemia.

Warnings, Precautions and Contraindications. The following **warning/precaution** is listed:

- *Pregnancy*: Ribavirin may cause birth defects and fetal death, and animal studies have shown interferons have abortifacient effects; avoid pregnancy in female patients and female partners of male patients. Patients must have a negative pregnancy test prior to initiating therapy, use at least two effective non-hormonal methods of contraception, and have monthly pregnancy tests.

The following **contraindications** are listed:

- When used in combination with peginterferon alfa/ribavirin or ribavirin alone, all contraindications to peginterferon alfa and/or ribavirin also apply to Sovaldi combination therapy.
- Because ribavirin may cause birth defects and fetal death, Sovaldi in combination with peginterferon alfa/ribavirin or ribavirin is contraindicated in pregnant women, and in men whose female partners are pregnant.

Drug Interactions. Drugs that are potent intestinal P-

glycoprotein (P-gp) inducers (e.g., rifampin, St. John's Wort) may significantly reduce plasma concentrations of sofosbuvir and, thus, lead to a reduced therapeutic effect. Rifampin and St. John's Wort should not be used with Sovaldi. An extensive list of other drugs that may lead to potentially significant drug interactions with Sovaldi is included in the product's prescribing information. Consult the full prescribing information prior to use for potential drug-drug interactions.

Administration, Dosing, and Availability. The recommended dose of Sovaldi is one 400 mg tablet, taken orally, once daily with or without food for 12 to 24 weeks. Dose reduction with Sovaldi is not recommended. Sovaldi should be used in combination with ribavirin or with a combination of ribavirin and pegylated interferon. Used in combination with ribavirin, Sovaldi is recommended for up to 48 weeks or until the time of liver transplantation, whichever comes first, to prevent post-transplant HCV reinfection. The product is available as tablets containing 400 mg sofosbuvir. It should be dispensed in its original container.

Patient Counseling Information. Specific points for patient counseling are summarized in Table 5.

Overview and Summary

The four new drugs are indicated to treat a wide variety of pathologies. In each case, the drugs have been shown to be effective and safe when used as directed. Each offers advantages over earlier treatments used to manage the respective disease states.

The author, the Ohio Pharmacists Foundation and the Ohio Pharmacists Association disclaim any liability to you or your patients resulting from reliance solely upon the information contained herein. Bibliography for additional reading and inquiry is available upon request.

This lesson is a knowledge-based CE activity and is targeted to pharmacists in all practice settings.

Program 0129-0000-14-006-H01-P
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CE Hours: 1.5 (0.15 CEU)

The Ohio Pharmacists Foundation Inc. is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

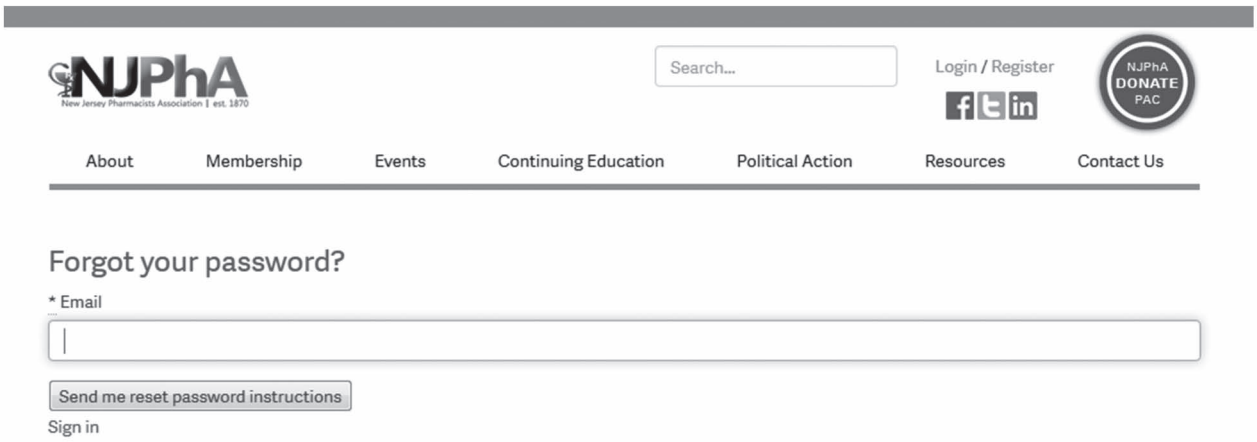
New Drugs: Aptiom, Imbruvica, Luzu, and Sovaldi CE exam on the following page

New Website Password Reminder

If you did not respond to the email notice to change your password, please reset your password to ensure you can access all the member features and program discounts.

Your user name is automatically set as the email address on file. Without a new password (you create it so you can remember it), the system will be unable to display member features and discounts.

Enter this URL in your browser and you will be sent a link with the reset password instructions. http://njpharmacists.org/users/password/new



continuing education quiz

New Drugs: Aptiom, Imbruvica, Luzu and Sovaldi

1. What percentage of people with epilepsy continues to have seizures despite treatment with more than one antiepileptic drug?
   a. 5-10 c. 20-30
   b. 10-20 d. 30-40

2. All of the following statements about Aptiom are true EXCEPT:
   a. its precise mechanism of action is unknown.
   b. it may cause suicidal thoughts and behavior.
   c. sodium levels should be monitored.
   d. taken with phenobarbital, a lower dose of Aptiom may be necessary.

3. The maximum daily recommended maintenance dose of Aptiom is:
   a. 200 mg. c. 1200 mg.
   b. 600 mg. d. 1500 mg.

4. All of the following are true statements about mantle cell lymphoma EXCEPT:
   a. it is a rare, aggressive form of non-Hodgkin lymphoma.
   b. it represents about 2 percent of all non-Hodgkin lymphoma.
   c. about 2,900 new cases are diagnosed in the U.S. each year.
   d. by the time it is diagnosed, it has usually spread to the lymph nodes.

5. Imbruvica is indicated for treatment of patients with mantle cell lymphoma who:
   a. are resistant to ribavirin and peginterferon alfa.
   b. have received at least one prior therapy.
   c. are free of serious systemic fungal infections.
   d. are six years of age and older.

6. The adverse reaction most frequently leading to treatment discontinuation with Imbruvica was:
   a. diarrhea. c. anemia.
   b. subdural hematoma. d. bruising.

7. All of the following are true statements about tinea infections EXCEPT:
   a. they are found worldwide.
   b. they may interfere with sleep.
   c. their incidence has increased since 2005.
   d. they are anthropophilic infections.

Completely fill in the lettered box corresponding to your answer.

1.	[a]	[b]	[c]	[d]	6.	[a]	[b]	[c]	[d]	11.	[a]	[b]	[c]	[d]
2.	[a]	[b]	[c]	[d]	7.	[a]	[b]	[c]	[d]	12.	[a]	[b]	[c]	[d]
3.	[a]	[b]	[c]	[d]	8.	[a]	[b]	[c]	[d]	13.	[a]	[b]	[c]	[d]
4.	[a]	[b]	[c]	[d]	9.	[a]	[b]	[c]	[d]	14.	[a]	[b]	[c]	[d]
5.	[a]	[b]	[c]	[d]	10.	[a]	[b]	[c]	[d]	15.	[a]	[b]	[c]	[d]

❑ **I am enclosing $5 for this month's quiz made payable to: Ohio Pharmacists Association.**

1. Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
2. Did it meet each of its objectives? ❑ yes ❑ no
   If no, list any unmet_____
3. Was the content balanced and without commercial bias?
   ❑ yes ❑ no
4. Did the program meet your educational/practice needs?
   ❑ yes ❑ no
5. How long did it take you to read this lesson and complete the quiz? _____
6. Comments/future topics welcome.

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Return quiz and payment (check or money order) to Correspondence Course, OPA, 2674 Federated Blvd, Columbus, OH 43235-4990

8. Which of the following is appropriate patient advice for Luzu cream?
   a. Apply a thin layer to affected skin areas and to about one inch of the surrounding healthy skin.
   b. Squeeze one inch of cream onto the affected area only.
   c. Avoid exposure to sunlight, incandescent lights and excessive heat.
   d. Avoid concomitant use of cosmetic skin lightener ointments and creams.

9. All of the following statements are appropriate in counseling patients on Sovaldi EXCEPT:
   a. do not drive or operate heavy machinery while taking Sovaldi.
   b. take with or without food.
   c. store Sovaldi in its original container.
   d. it should not be used during pregnancy.

10. Which of the following drugs inhibits Bruton's tyrosine kinase?
   a. Aptiom c. Luzu
   b. Imbruvica d. Sovaldi

11. Which of the following drugs was approved to be used in combination with ribavirin or ribavirin and peginterferon alfa?
   a. Aptiom c. Luzu
   b. Imbruvica d. Sovaldi

12. Which of the following drugs was approved with orphan-product designation?
   a. Aptiom c. Luzu
   b. Imbruvica d. Sovaldi

13. Seventy percent of chronic hepatitis C virus infections in the U.S. are caused by which of the following HCV genotypes?
   a. 1 c. 3
   b. 2 d. 4

14. All of the following drugs are taken orally EXCEPT:
   a. Aptiom. c. Luzu.
   b. Imbruvica. d. Sovaldi.

15. The label of which of the following drugs lists no warnings, precautions or contraindications?
   a. Aptiom c. Luzu
   b. Imbruvica d. Sovaldi

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