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Special Points of Interest:

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EDITORS:

Andre Emont,
Pharmacy Director

Victor Pardo,
Operations Manager

Michael Chu,
Clinical Pharmacy Manager

Nishat Faruqui,
Clinical Pharmacist

Helen Horng,
Clinical Pharmacist

Gregory Eilinger,
Clinical Pharmacist

Merlin Punnoose,
Clinical Pharmacist

Clement Chen,
Clinical Pharmacist

Arun Mattappallil,
Clinical Pharmacist

Joshua Colorado
Clinical Pharmacist

Maryam Zaeem
Clinical Pharmacist

Jaclyn Scalgione
Clinical Pharmacist

P&T Update

Formulary Additions

Nusinersen (Spinraza®) Formulary Addition Request – Approved.

- Nusinersen is an orphan drug FDA approved for spinal muscular atrophy (SMA) in pediatric and adults. – Dr. Chetan Malik approved in addition to Dr. Bach and Dr. Kornitzer as an authorizing physician for nusinersen ordering.
- **Levonorgestrel (Liletta®) intrauterine device (IUD), Copper (Paragard T380A®) IUD, Etonorgestrel (Nexplanon®) implant** – Formulary addition approved with the restriction criteria.
- **Acetaminophen IV (Ofirmev®) – Formulary Restriction**
  Drafting of updated restriction criteria to include approval by anesthesiology for orders longer than 24-48 hours unanimously approved – Agreement to draft an updated restriction workflow and bring back to October P&T for final approval.
- **Meningococcal Group B Vaccine (Bexsero®) – Formulary Addition Request**
  Formulary addition unanimously approved for approval with amended motion for use in patients ages 10 or older – Addition approved.

Formulary Deletions

- Tolnaftate 1 % cream/solution – Formulary Deletion – Approved
- Glatiramer (Copaxone®) – Formulary Deletion – Approved
- Pioglitazone (Actos®) 30mg, 45mg – Formulary Deletion – Approved
- Buprenorphine/ Naloxone (Suboxone®) – Formulary Deletion – Approved
- Hydrocortisone Valerate Cream & Ointment – Formulary Deletion – Approved
- Collodial Bath Granules – Formulary Deletion – Approved
- Calcipotroene 0.005% Cream – Formulary Deletion – Approved
- Mafenide Cream & Solution – Formulary Deletion – Approved
- Benzoyl Peroxide 5% – Formulary Deletion – Approved
- Dibucaine 1% – Formulary Deletion – Approved
- Imipramine 50mg Tab – Formulary Deletion – Approved
- Triple Dye – Formulary Deletion – Approved
- Tiagabine 2mg & 4mg Tabs – Formulary Deletion – Approved
- Amvisc® – Formulary Deletion – Approved
- Vitamin C oral liquid – Formulary Deletion – Approved
- Triamterene 50mg Capsule (Dyrenium®) – Formulary Deletion – Approved
- Sotalol IV – Formulary Deletion – Approved

Line of Extension Approvals

- Hepatitis B Vaccine (Engerix-B®) – Line of Extension – Approved
- Sodium Hyaluronate 0.85mL (Provisc®) – Line of Extension – Approved

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P&T Updates
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Policies & Procedure/Floor stocks Updated

- Automatic Stop Order Policy updated – 707-600-103.
  An update on the policy to change the default stop order time of piperacillin- tazobactam to 3 days from 7 days in Epic was presented. – Approved.
- 707-400-117 Use of Biosimilars, Therapeutic Interchange of Biosimilars – Approved.
- 707-500-122 Automatic Therapeutic Exchange Policy – Updated
  The addition of Buprenorphine/Naloxone (Suboxone®) autosubstitution to buprenorphine – Approved.
- 707-600-117 Investigational Drug Services Policy – Updated Policy – Approved.

Nivolumab Improves Survival in Recurrent Squamous-Cell Carcinoma of the Head and Neck

Nivolumab (Opdivo®) is an anti-programmed death receptor 1 (PD-1) monoclonal antibody, which inhibits the binding of the PD-1 ligand that inhibits the T-cell—suppressive immune-checkpoint receptor PD-1 which can be used as a primary second line treatment after first-line platinum based therapy treatment of recurrent squamous-cell carcinoma of the head and neck (HNSCC) has failed.

When cancer progresses within 6 months after treatment with platinum-based therapy, patients have a median survival of 6 months or less. More than 50% of patients have a recurrence of the disease within 3 years, which is mediated by immune evasion. Nivolumab was approved for the use in HNSCC after the CHECKMATE 141 study. This study compared the use of nivolumab to standard therapy after platinum-based therapy has failed in patients with HNSCC. Methotrexate, docetaxel, or cetuximab were given to the patients who were in the standard therapy group. The median overall survival in the nivolumab group was 7.5 months compared to 5.1 months in the standard therapy group (95% confidence interval [CI], 5.1 to 9.1). Nivolumab was associated with a statistically longer overall survival than standard therapy by reducing the risk of death by 30% (hazard ratio for death of 0.70, 97.73% CI, 0.51 to 0.96, p=0.01). When comparing estimates of 1-year survival rates, patients in the nivolumab group were estimated to have a 36.0% chance of survival compared to 16.6% chance in the standard therapy group. At 6 months, progression-free survival was 19.7% with nivolumab and 9.9% with standard therapy. The response rate to the nivolumab versus the standard treatment were 13.3% versus 5.8%, respectively. Nivolumab was also associated with a better quality of life with respect to less pain, less difficulty swallowing, and less degradation in physical, emotional and social functioning through the duration of the treatment, as compared to the standard therapy group.

Based on the results of this study, the National Comprehensive Cancer Network (NCCN) updated their guidelines for treatment of HNSCC to state that upon failure of platinum-based first-line therapy, physicians should use nivolumab as the first-choice of second-line treatment. PD-1 inhibitors are changing the approach to treating various cancers due to their increased efficacy, favorable side effect profile over traditional therapies and extended survival rate.

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Contributed by:
Danielle Maffei, PharmD Candidate Class of 2018
St. John's University College of Pharmacy and Health Sciences

Gabapentin & Abuse Potential

Gabapentin, an anticonvulsant commonly used to treat epilepsy and neuropathy, is increasingly being misused and abused by patients. Physicians have been prescribing this medication excessively as a safer alternative to opioids, likely in response to the opioid epidemic. With 57 million prescriptions written in 2015 alone, overprescribing of this medication is at an all-time high in the US. However, many people are unaware of the abuse potential associated with it because it is not currently scheduled as a controlled substance in most US states.

Gabapentin is structurally related to the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), but does not bind to its receptors. High-affinity gabapentin binding sites in the brain are associated with voltagegated calcium channels that modulate the release of excitatory neurotransmitters and play a role in epileptogenesis and nociception. Currently, gabapentin is not scheduled throughout the US, but pregabalin (Lyrica), another gabapentinoid with a similar structure and pharmacokinetic activity, is a Scheduled V controlled substance. In addition, gabapentin shares many of the same properties as abused intoxicants and can produce psychoactive effects and withdrawal with high doses and abrupt discontinuation.

Known by its street names *morontin* and *gabbies*, this drug acts as a mild tranquilizer creating feelings of calmness and sociability. When taken alone, gabapentin's abuse potential is minimal. However, when taken with other drugs like opioids, muscle relaxers or anxiolytics, the risk of abuse and addiction significantly increases, potentiating CNS effects such as drowsiness and sedation and creating a state of euphoria similar to the high produced by cannabis. One study derived from law enforcement data between 2002 and 2015 found that abusers were taking gabapentin in conjunction with opioids to prolong the duration of the high. Users have reported taking doses of 900-2400 mg to achieve an opioid high. It has also been found as a cutting agent in heroin, resulting in accidental overdoses. Case reports have also found daily doses prescribed as 4800 mg, due to tolerance, and 1800 mg increased by patients to 7200 mg and 4900 mg respectively, resulting in hospitalizations and severe withdrawals. According to a presentation at the 68th AACC Annual Scientific Meeting & Clinical Lab Expo in Philadelphia, 1 in 5 patients who used opioids for pain tested positive for gabapentin even though they did not have a prescription for it. In addition, the Drug Abuse Warning Network states that the number of emergency department visits for gabapentin misuse and abuse in cities has increased by nearly five times from 2008 to 2011.

Last year, the Advisory Council on the Misuse of Drugs (ACMD) in the UK recommended the

reclassification of gabapentin, along with pregabalin, to a Class C controlled substance placed under Schedule 3 prescribing regulations. This means they will not be able to be repeat-dispensed and prescriptions will only be valid for one month. Also, Ohio has recently acknowledged gabapentin as an abusive drug that must be monitored. To support this, in December 2016, the State of Ohio Board of Pharmacy required all pharmacies, wholesalers and physicians to report when any product containing gabapentin is dispensed to the Ohio Automated RX Reporting System. Minnesota, Virginia, Illinois, Wyoming, and Massachusetts also have new prescription monitoring programs for this drug. Lastly, Kentucky became the first state to make gabapentin a schedule V controlled substance in July 2017.

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Gabapentin & Abuse Potential

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Although it is not considered to be abusive when used as monotherapy for its proper indications, recreational use of gabapentin, especially at doses higher than recommended, is extremely dangerous when used with other depressants. gabapentin is easily abused and can lead to withdrawal and dependence, resulting in severe CNS side effects, possible respiratory failure and even death. Already being reclassified and monitored in some states, we are likely to see more states making Gabapentin a controlled substance due to its abuse potential and illicit use.

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Contributed by:
Kristina Bruno, St. John's University, Pharm D. Candidate 2018

Analyzing the Impact of the *Burkholderia cepacia* Outbreak in PharmaTech Facilities

The Centers for Disease Control and Prevention (CDC), in collaboration with the Food and Drug Administration (FDA) and state and local health departments, recently conducted a public health investigation on the recent multistate outbreak of *Burkholderia cepacia*. This outbreak affected 63 hospitalized patients in 12 states.[1] The search detected B. cepacia in the water system and revealed contamination in more than ten lots of oral liquid docusate sodium manufactured by PharmaTech LLC, Davie, Florida.[1,2]

On August 2, 2017, Rugby Laboratories issued a voluntary nationwide recall of Diocto Liquid and Diocto Syrup manufactured by PharmaTech, LLC. Diocto Liquid was nationally distributed to wholesale and retail facilities, including hospitals and pharmacies, and the FDA received several adverse event reports of *B. cepacia* infections which may be due to the contaminated Diocto products.[3] According to the recall letter, consumers, pharmacies, and healthcare facilities were to stop using and dispensing the product immediately. In addition, as a precautionary measure, another nationwide voluntary recall was issued of all liquid products manufactured by PharmaTech at its facility in Davie, FL due to possible product contamination.[4] The recall included items such as liquid multivitamin supplements, Senna syrup, Certa-Vite Liquid, Poly-Vita Drops, ferrous sulfate elixir, calcionate syrup, and D3 400 IU liquid with a total of 22 over-the-counter liquid medications.[4] These products were labeled under Rugby Laboratories, Major Pharmaceuticals, and Leader Brands.

B. cepacia is a group of bacteria that is found in soil and water. It can be transmitted via person-to-person contact, contact with contaminated surfaces, or exposure to the bacteria in the environment.[5] Although these bacteria pose very little medical risk to healthy individuals, people who have a weakened immune system or serious illnesses, such as cancer, acquired immune deficiency syndrome (AIDS), cystic fibrosis, or other chronic lung diseases, are more susceptible.[5,6]

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Analyzing the Impact of the *Burkholderia cepacia*

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The effects of *B. cepacia* vary, ranging from no symptoms to serious respiratory infections. Other symptoms include increased cough, congestion, dyspnea, and possible fever.[6] Cepacia syndrome, which is characterized by high fever, severe progressive respiratory failure, leukocytosis, and increased erythrocyte sedimentation rate, is also possible.[7] However, not all types of *B. cepacia* are associated with this syndrome. Among the *B. cepacia* complex, some – *B. cenocepacia* and *B. dololsa* – can be more harmful than others.[6] Treating *B. cepacia* infections can be difficult as the species of bacteria are often resistant to many antibiotics. However, some types of *B. cepacia* are sensitive to trimethoprim-sulfamethoxazole, doxycycline, ceftazidime, and meropenem.[6] Nevertheless, decisions on the treatment of infections with *B. cepacia* should be made on a case-by-case basis.[5]

B. cepacia contamination in pharmaceutical products is not a matter that can be disregarded. It must be addressed immediately as it can lead to very serious respiratory issues and life-threatening conditions. A representative for PharmaTech was contacted but declined to comment beyond the recall notice. It is unclear what actions the manufacturer is taking to rectify this issue and there has been no formal announcement regarding future product shipment. Any adverse reactions, quality problems, or suspicion of patient infection possibly associated with the use of the products mentioned in the recall notice should be reported to the FDA's MedWatch Adverse Event Reporting program.[1]

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Contributed by:
Pranjal Patel, Pharm D Candidate, Class of 2018
Rutgers Ernest Mario School of Pharmacy

Therapeutic Implications of the Increased Risk of Amputations Associated with Canagliflozin Therapy

Invokana (canagliflozin) is a sodium-glucose co-transporter 2 (SGLT2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Available in multiple products such as Invokana, Invokamet, and Invokamet XR, canagliflozin offers a new option for patients with type-2 diabetes. Canagliflozin was first approved by the FDA on March 29, 2013 to treat hyperglycemia in type-2 diabetes, being first in its class with the novel mechanism of inhibiting the glucose reabsorption in the proximal tubules of the kidney. Specifically, canagliflozin blocks the SGLT-2 receptors found predominantly on the S1 segment of the proximal renal tubule causing glucosuria. Canagliflozin results in 0.5-1.0 % HgA1c reduction, with several advantages such as low risk of hypoglycemia, weight loss, and reduction in blood pressure.

In an effort to assess the safety and efficacy of canagliflozin, The Canagliflozin Cardiovascular Assessment Study (CANVAS) program integrated data from two trials involving a total of 10,142 participants with type-2 diabetes and high

cardiovascular risk. The results showed that patients who were treated with canagliflozin had significantly lower rates of the primary cardiovascular outcome than patients assigned to placebo. However, the study showed a new finding: a higher risk of amputation of toes, feet, or legs with canagliflozin than with placebo (6.3 vs. 3.4 participants with amputations per 1000 patient-years). The CANVAS trial found the risk was higher in individuals who had history of amputations or other risk factors.

On May 16, 2017, the FDA issued a warning regarding the increased risk of leg and foot amputation associated with the use of canagliflozin based on the results of the CANVAS trials. Healthcare professionals are advised to exercise appropriate clinical judgement and consider factors that may predispose patients to amputations such as history of prior amputation, peripheral vascular disease, neuropathy, and diabetic foot ulcers. The FDA recommends that patient on canagliflozin therapy be monitored for any signs and symptoms of infection, pain, tenderness, sores, or ulcers. If any of these complications occur, the FDA recommends discontinuation of canagliflozin therapy in said patient. Healthcare professionals are to inform patients of the increased risk of amputation associated with the use of canagliflozin.

Overall, it is important for prescribers to weigh the risks and benefits when considering canagliflozin therapy. Patients should have a thorough history to determine risk factors for amputation. In addition, patient should be assessed for capacity to report signs and symptoms of foot infection.

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Contributed by:
Sara Massak
2018 Pharm.D. Candidate
Fairleigh Dickinson School of Pharmacy & Health Sciences

FDA Issues Black-Box Warnings Regarding Concomitant Use of Opioids and Benzodiazepines

Two classes of central nervous system (CNS) depressants, benzodiazepines and opioids, carry severe risks when administered together and the U.S. Food and Drug Administration (FDA) has released guidance on how to manage the potential for additive CNS depression. Concomitant use of CNS depressants has proven to be an issue as a study published in the *American Academy of Forensic Sciences* cited previous studies' findings that benzodiazepine consumption was found in 11% to 86% of opioid-related deaths[1].

Although the mechanism of action of benzodiazepines has not been fully illuminated, the class of anxiolytics presumably exert their pharmacologic action via gamma-aminobutyric acid, commonly referred to as GABA[2]. Benzodiazepines act at multiple levels of the CNS to produce effects such as anxiolysis, sedation, hypnosis, muscle relaxation, and amelioration of convulsions[2]. These intended effects give benzodiazepines tremendous utility, but can be exacerbated when administered alongside agents that precipitate similar action, such as opioids.

Unlike benzodiazepines, opioids have a fully elucidated mechanism of action and bind centrally to muopioid receptors to decrease the ability to perceive pain[3]. Opioids are a mainstay in treatment of moderate-severe pain and are highly effective when used appropriately. One major confounder to the use of opioids is the absence of a maximum daily dose. Because pain and its tolerance are inherently individualized, the overarching recommendation for dosing opioids is to titrate to pain control, with no maximum dose recommendations[4]. For patients experiencing tachyphylaxis to opioids, they require increased doses to control pain. At higher doses, patients become more at risk for side effects such as respiratory depression and even death. Opioids alone can severely diminish a patient's respiratory drive and when used in combination with other CNS depressants, such as benzodiazepines, the risk is even greater.

On August 31, 2016, the FDA released a black-box warning regarding the concomitant use of opioids and benzodiazepines, which states, "Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma and death. Reserve concomitant prescribing for patients with inadequate alternative treatment options. Limit dosages and durations to the minimum required and follow patients for signs and symptoms of respiratory depression and sedation."[5] The verbiage stipulates that prescribers

should only order the two drugs in combination when absolutely necessary, and that patients should be vigilantly monitored for adverse reactions. While the black-box warning specifies benzodiazepines and opioids, care should also be taken with any combination of CNS depressants, including ethanol, hypnotics, muscle relaxants, anti-psychotics, and barbiturates.

Regarding the use of medication-assisted treatment (MAT) drugs—e.g. methadone and buprenorphine, both of which bind to the muopioid receptor—the FDA released a memo on September 20, 2017, stating, "…opioid addiction medications [such as] buprenorphine and methadone should not be withheld from patients taking benzodiazepines or other drugs that depress the CNS."[6] The FDA recommends patient education, tapering to discontinuation when possible and coordinating care with other prescribers as methods to limit concomitant use of MAT drugs and other CNS depressants6.

Care should be taken when prescribing and administering multiple CNS depressants, and adherence to FDA recommendations will help ensure patients are exposed to minimal risk.

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FDA Issues Black-Box Warnings Regarding Concomitant

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Contributed by:
Jason Voss, PharmD/MBA Candidate, Class of 2018
Fairleigh Dickinson University School of Pharmacy and Health Sciences

Oral Anticoagulants Overview and Reversal Agents Considerations

In the past decade, four new Direct Oral Anticoagulants (DOACs) had entered US market. The prescribing of these newer anticoagulants has steadily increased. Compare to warfarin, there is uncertainty relating to optimal laboratory monitoring, perioperative management and treatment of bleeding.

Warfarin inhibits vitamin K epoxide reductase and prevents formation of clotting factors II, VII, IX, X. Dabigatran is a direct thrombin inhibitor (DTI). Rivaroxaban, apixaban, Edoxaban are factor Xa inhibitors. They all work by interrupting the coagulation cascade and have shown similar efficacy to warfarin for FDA approved indications.

There are few coagulation assays that might have clinical utility for DOAC monitoring. aPTT/PT for dabigatran with some dose response but less reliable at higher concentration; ecarin clotting time (ECT) which provides reliable, concentration dependent, linear response to DTI[i]. PT/INR provides linear dose response to factor Xa inhibitors but normal PT/INR can be seen in patients receiving therapeutic doses. Antifactor Xa assay provides highly reproducible and precise, dose-dependent linear response[ii] to factor Xa inhibitors.

Urgent reversal of oral anticoagulants includes fresh frozen plasma (FFP) and prothrombin complex concentrate (PCC). They aid in reversal but are not true antidotes. FFP are composed of both coagulation and anticoagulant factors in normal physiological concentrations. Recommended FFP reversal dose are 10 – 20 mL/kg. Two units should provide 20% – 30% increase in level of plasma clotting factors.[iii,iv] PCC used at University Hospital currently is Feiba® which is an activated PCC, it contain factors II, aVII, IX, X. UH will soon be converting to Kcentra® which also contain factors II, VII, IX X (major differences of the two products are factor VII is activated in Feiba® and heparin[v] is in Kcentra®).

Kcentra® is FDA approved for reversal of warfarin associated coagulopathy, dose recommended are 25-50 unit/kg based on presenting INR. It is critical to concurrently administer phytonadione IV due to 5 half-life of warfarin is one week and PCC effect only last hours. PCC is not approved for reversal of newer DOACs. Case reports on PCC efficacy for DOAC reversal are inconsistent with wide dosing range used. Thrombotic risk with PCC use versus hemorrhagic shock must be weighted in any off label indications.

Idarucizumab is FDA approved antidote for dabigatran only. It's binds and neutralizes dabigatran to allow normalization of clotting parameters.[vi,vii] Timing of last dabigatran dose is important to evaluate if any dabigatran is present for Idarucizumab to bind and reverse.

Andexanet alfa is not FDA approved yet, it is a factor Xa inhibitor antidote, a recombinant modified factor Xa decoy molecule. It competes with circulating factor Xa to bind directly with factor Xa inhibitors as well as

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Oral Anticoagulants Overview

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heparin-antithrombin complexes and therefore inhibits both direct and indirect factor Xa inhibitors effect of anticoagulation.[viii] Based on currently available trial data, different dosing is recommended for different factor Xa inhibitors needing reversal.[ix,x]

Ciraparantag/Aripazine is not FDA approved yet, it is being investigated as "universal" reversal agent for multiple anticoagulants (unfractionated heparin, low molecular weight heparin, argatroban and DOAC). Ciraparantag directly binds to anticoagulants.[xi]

As with any medication, use of reversal agents such as PCC must be weighted again risk of thrombosis. Keep in mind, patients presented with bleeding while on anticoagulants has elevated thrombotic risks. PCC administration will further elevate the acute risk for thrombosis.

Medication	**class**	**Half-life normal renal**	**Reversal agents**	**Reversal Dosing**	**Time lapse from last dose for reversal agent consideration with Life threatening bleeds** *normal renal function, dose
Heparin	UFH	1.5 hrs (1-2 hrs)	Time, protamine	4.5 – 7.5 hrs reversal agent not needed 1mg neutralizes 100 units heparin	< 4 hrs
Warfarin	VKA	40 hrs (20-60hrs)	Vitamin K, PCC (Kcentra®)	VK: 10 mg IV x1 may repeat in 8-12 hrs INR 2- <4: 25 units/kg kcentra max 2500 in ICH INR 2- <4: 25 units/kg kcentra max 2500 in ICH INR 4- 6: 35 units/kg kcentra max 3500 in ICH INR > 6: 50 units/kg kcentra max 5000 in ICH *500-1000 units for emergent surgery for ICH?	Use INR for decision making in acute life threatening ICH, close space bleed
LMWH	LMWH	6 hrs (4.5 – 7 hrs)	Time, protamine	> 18 – 30hrs reversal agent not needed 1mg neutralizes 1 mg enoxaperin	< 18 hrs
Argatroban	DTI	45 min (39- 51 min)	Time, FFP Ciraparantag?		< 2 hrs
Bivalirudin	DTI	25 min	Time, FFP Ciraparantag?		< 75 min – 2 hrs
Dabigatran	DTI	15 hrs (12-17 hrs)	Idarucizumab; FFP, Ciraparantag? PCC?	2.5 Gm q15min x 2; 10-20 mL/kg	< 2 days
Rivaroxaban	FXa inhibitor	7 hrs (5-9 hrs)	FFP, PCC? Ciraparantag?	10-20 mL/kg	< 24 hrs
Apixaban	FXa inhibitor	12 hrs	FFP Ciraparantag? PCC?	10-20 mL/kg	< 36 hrs
Edoxaban	FXa inhibitor	12 hrs (10-14 hrs)	FFP Ciraparantag? PCC?	10-20 mL/kg	< 36 hrs

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Contributed by:
Helen S. Horng, PharmD., BCCCP, BCPS
Clinical Pharmacy Specialist

2017 Hypertension Guidelines

Introduction

Hypertension is a modifiable risk factor for multiple diseases including stroke, heart attack, and kidney disease. Numerous studies have shown a linear link between increased blood pressure and cardiovascular risk. In November 2017 The American College of Cardiology/American Heart Association Task Force of Clinical Practice Guidelines released an update to the hypertension guidelines.[1-3] The updated guidelines focus on a new classification system, proper blood pressure monitoring techniques, and new targets for initiating drug therapy.

Blood Pressure Classification & Monitoring

The new blood pressure classification no longer includes a prehypertension category. The four categories are normal, elevated, stage 1 hypertension, and stage 2 hypertension.[1]

Normal: less than 120/80 mmHg

Elevated: systolic blood pressure (SBP) between 120-129 and diastolic blood pressure (DBP) less than 80 mmHg

Stage 1 hypertension: SBP between 130-139 or DBP between 80-89 mmHg

Stage 2 hypertension: SBP at least 140 or DBP at least 90 mmHg

More people will be classified with hypertension since the classification of hypertension is lower than in previous guidelines; however this does not necessarily mean more patients should be taking medication.[1] The new guidelines emphasize proper blood pressure monitoring in the healthcare setting, as well as at home. They recommend having the patient avoid smoking, caffeine, or exercise 30 minutes prior to the measurement, ensuring that the patient remains sitting for 5 minutes directly prior to the measurement, supporting the limb used to measure blood pressure, and ensuring the cuff is at heart level. They state that practitioners should take the average of 2-3 measurements on 2-3 separate occasions to provide a more accurate estimate. The guidelines also encourage self monitoring by patients at home. Patients should follow the same procedures for monitoring blood pressure as in the office setting and use the same instrument for each measurement in order to accurately compare results.

Treatment of Hypertension

Those with normal blood pressure should continue to follow optimal lifestyle habits while those with elevated blood pressure should follow nonpharmacologic therapy. Nonpharmacologic therapy includes weight loss, a diet rich in fruits, vegetables, and whole grains, regular physical activity, and 1-2 drinks per day depending on gender.

The use of patients' cardiovascular risk is another major update to the 2017 guidelines. Stage 1 hypertension is treated with nonpharmacologic therapy along with medication, only if indicated based on a cardiovascular risk factors. Cardiovascular risk factors are based on clinical atheroschlerotic cardiovascular disease (ASCVD) or an estimated 10-year cardiovascular disease (CVD) risk more than 10%. Patients with stage 1 hypertension and diabetes or chronic kidney disease are also placed in the high risk category requiring medication therapy. Stage 2 hypertension is treated with nonpharmacologic therapy and blood pressure lowering medication, regardless of cardiovascular risk factors, when blood pressure is more than 20/10 mmHg higher than their target. The use of cardiovascular risk factors help determine whether a patient will require blood pressure lowering medication in addition to nonpharmacologic therapy in hypertension stages 1-2.[2-3]

Most patients can aim for a blood pressure target of less than 130/80 mmHg, regardless of known cardiovascular disease. The guidelines do state that a lower target may be reasonable in certain populations such as those with a higher risk for CVD. In stage 1 hypertension, practitioners should initiate therapy with a single first-line agent. In stage 2 hypertension, practitioners should initiate therapy with 2 first-line agents of different classes. First-line agents include thiazide diuretics, angiotensin-converting enzyme inhibitors (ACEi) or angiotensin-receptor blockers (ARBs), and calcium channel blockers (CCB). In the thiazide category, chlorthalidone is preferred over other agents such as hydrochlorothiazide and metolazone based on half life and proven reduction of cardiovascular disease. Patients on thiazide diuretics should have calcium levels, uric acid levels, and electrolytes monitored. Practitioners should not recommend

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ACEi, ARBs, or direct renin inhibitors (aliskiren) in combination with each other. ACEi, such as lisinopril and quinapril, and ARBs, such as losartan and valsartan, can cause hyperkalemia in those taking potassium supplements or potassium-sparing diuretics. These agents may also cause acute renal failure and patients at risk should be closely monitored. Additionally, patients should discontinue ACEi/ARBs during pregnancy. Calcium channel blockers consist of dihydropyridines and nondihydropyridines. Dihydropyridines (such as amlodipine, nifedipine) are more likely to cause lower extremity edema. Use of nondihydropyridines (diltiazem and verapamil) should be monitored for drug interactions and should not be used in heart failure patients with reduced ejection fraction. Beta blockers are not recommended as first-line agents for hypertension, but may be considered in patients with other indications such as heart failure or ischemic heart disease. For patients with concomitant hypertension and heart failure with reduced ejection fraction, the preferred beta blockers include bisoprolol, metoprolol succinate, and carvedilol. Secondary agents for hypertension include loop diuretics, potassium sparing diuretics, aldosterone antagonists, and alpha blockers which can all be considered for patients with specific indications.

While the 2017 guidelines take into account the results of newer clinical trials since the last update, it will be interesting to see how the updated guidelines change clinical practice in the coming years. Despite any changes, the updated guidelines indicate that we are moving towards better cardiovascular health by compiling incoming research and empowering patients to manage their own health.

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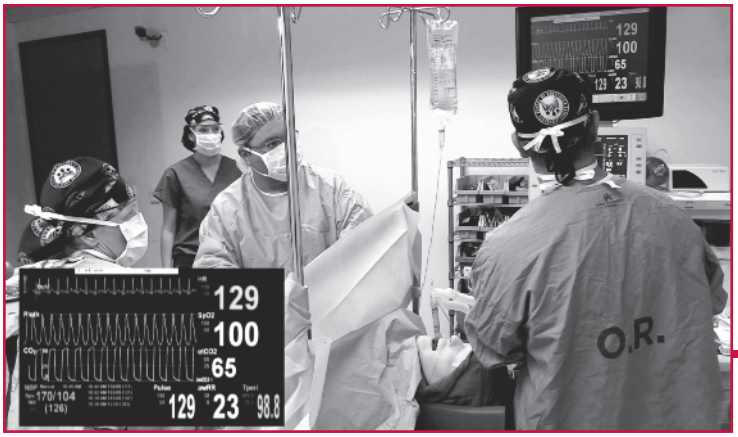
Contributed by:
Brittany Yalamanchili, Pharm.D.

Malignant Hyperthermia (MH) Mock Drill in the Operating Room (OR) at University Hospital

One of The Joint Commission (TJC) recommendations is to hold periodic training exercises to keep the staff in tune with the management of malignant hyperthermia patients, since it is a rare but serious entity.

Back in March 2017, the anesthesia dept. conducted a MH Mock Drill. Five ORs were booked with two mock patient case scenarios in each. The anesthesia and the OR PCS departments participated. The clinical pharmacist served as an evaluator along with other anesthesia providers and recorded the matrices for different interventions. The mock patients received anesthesia and experienced



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Malignant Hyperthermia (MH) Mock Drill

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malignant hyperthermia episode (temp. > 103F, muscle rigidity, tachycardia, acidosis, multiorgan failure). The team leader walked the team through different steps on the identification and systematic management of hyperthermia, dantrolene administration, antiarrhythmic institution, laboratory orders, calling MH hotline and notification to the ICU. Any issues/deficiencies were identified to further better the patient care, and optimize the team dynamics. Some of the areas for improvements identified were for personnel to bring code cart/anesthesia cart together, instituting read back on the interventions performed; clear delineation of the roles such as mixing of medications, supplying ice to cool the patient, notification of ICU/MH hotline etc. Also, it was identified was that the dantrolene vials needed to be reconstituted and administered constantly until the full dose was given and the full dose needed to be repeated until the resolution of symptoms or reaching the maximum cumulative dose.

The evaluation matrices for the drill were both objective and subjective. The objective assessment included time to bring the code/MH carts, time to administer the first vial and full dose of dantrolene, time to draw and assess lab results, time to notify MH hotline/ICU and time to patient stabilization. The subjective parameters assessed were: collaborative and coordinated team efforts with a designated team leader, participant feedback, reminders from the staff if any critical steps were missed, and overall team experience with the drill. The staff provided a positive feedback with the training exercise and expressed enthusiasm to conduct further drills to facilitate an environment conducive to the staff learning and advancement.

The drill was a success and achieved a meaningful training environment for the OR staff. It showed the productive collaboration and hard work on part of anesthesia, pharmacy and PCS. The drill needs to be undertaken periodically to keep the staff abreast of the MH management and similar training exercises in other areas using paralytics such as ER/PACU/ICU need to be pursued.

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Contributed by:
N. Faruqui, RPh, Pharm D, BCPS

Mr. Andre Emont - Certified Joint Commission Professional (CJCP®)

Congratulations to Mr. Emont on passing the CJCP® examination and is now a Certified Joint Commission Professional CJCP®.

The testing included understanding The Joint Commission Accreditation process, Joint Commission Accreditation Standards, special focus on Medical Staff Standards, special focus on Environment of Care Standards, Leadership Skills, Performance Improvement and Patient Safety (including National Patient Safety Goals). Mr. Emont now joins 300+ accreditation professionals who have successfully earned their CJCP and his name is reflected on the Joint Commission Resources (JCR) website. Mr. Emont's CJCP certification is good for a three-year period until he must recertify. The CJCP credential proves Mr. Emont's dedication to Joint Commission standards and survey process as well as to supporting patient safety. It allows him not only professional growth but benefits the organization as well.

References:

- *Certified Joint Commission Professional*™ (CJCP®) Candidate Handbook 2017

Contributed by:
Michael Chu, Pharm. D.
Clinical Pharmacy Manager