Pharmacy News

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Newark, New Jersey

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Special Points of Interest:

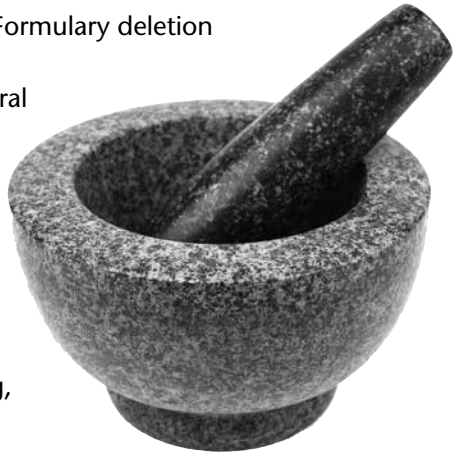
P&T Update

Formulary Additions

- **Translingual nitroglycerin spray (Nitrolingual®)**
  - Restrict use to EMS only
- **Apixaban (Eliquis®)**
  - Formulary addition approved
- **Basiliximab (Simulect®)**
  - Formulary addition approved
- **Anidulafungin (Eraxis®)**
  - Formulary addition approved
- **Glucose oral gel**
  - Formulary line extension approved – Restrict to ambulatory clinic kit use only.
- **Lidocaine**
  - topical jelly (Glydo®) Formulary line extension & auto-substitution approved
- **Cefuroxime axetil (Ceftin®)**
  - 250mg tablets- Formulary reinstatement approved
- **Factor VIII**
  - Antihemophillic factor recombinant (Xyntha® Solofuse) - Formulary line extension approved

Formulary Deletions

- All formulary deletion requests were approved for deletion (see below).
  - Rabies Immuneglobulin (HyperRab® & Imogam® 150 IU/ml) - Formulary deletion approved
  - Factor VIII Antihemophillic factor recombinant (Helixate®) - Formulary deletion approved (manufacture discontinue)
  - Nesiritide (Natrecor®) IV - Formulary deletion approved (manufacturer discontinue)
  - Zinc sulfate & chloride IV - Formulary deletion approved
  - Chloramphenicol IV - Formulary deletion approved
  - Cyclophosphamide (Cytoxan®) 50mg tab- Formulary deletion approved
  - Chlorzoxazone (Lorzone®) 500mg tab - Formulary deletion approved
  - Cefuroxime axetil (Ceftin®) 250mg/5ml oral liquid - Formulary deletion approved
  - Diclofenac (Voltaren®) 75mg tablet formulary deletion approved
  - Hydroxyzine pamoate (Vistaril®) salt form - Formulary deletion approved
  - Maraviroc (Selzentry®) 300mg tab - Formulary Deletion approved
  - MVI with fluoride (Poly-Vi- Flor®) 0.25mg, 0.5mg, 1mg tablets- Formulary deletion approved



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P&T Updates
(Continued from page 1)

- Nortriptyline (Pamelor®) 50mg capsule- Formulary deletion approved
- Timolol 5mg tablet- Formulary deletion approved

Policies & Procedure/Floor stocks

707-500-122 Automatic Therapeutic Exchange (ATEP) revision

- Fluorescein 0.6mg and 1mg strips depending on the product availability – approved by ophthalmology division - approved
- Lidocaine topical syringes Uro-Jet® and Glydo® are interchangeable – approved by urology - Approved

707-700-105A Intravenous med administration guideline revision

- Guideline revision to include phenylephrine IVP by physician in MICU & ED – Approved

Miscellaneous

- Anticoagulation reversal agents approving gatekeeper modification request extending emergency department attending and cardiology attendings
- Alaris Drug Library revision – Approved

Antiretroviral Therapy During Pregnancy: Updates in Dolutegravir (Tivicay) Use

Background:

In the United States, the guidelines for HIV treatment are created by the Department of Health and Human Services (HHS) for variety of patient populations. According to the Perinatal Guidelines, treatment in pregnant women is based on whether a woman is currently receiving antiretroviral therapy. If a woman is receiving antiretroviral therapy, their regimen should be continued if they have achieved adequate viral suppression (viral load < 20 copies/mL). Patients who are antiretrovirals naive are recommended to start therapy.[1]

Typically, three different medications are used for treatment - two nucleoside reverse transcriptase inhibitors (NRTI) and any one agent from the following classes: protease inhibitors (PIs), non-nucleoside reverse transcriptase inhibitor (NNRTIs), or integrase inhibitors (INSTIs). Below is a medication guide defining the preferred and alternative HIV treatments for pregnant patients. Alternative agents are not first-line therapy for antiretroviral naïve patients but are acceptable for use under circumstances such as resistance, medication availability, or other patient specific factors. When using medications from the alternative category, it is still recommended to have two agents from the NRTI class (either a preferred or alternative agent) and one agent from another class (a PI, NNRTI, or INSTI).[1]

Issues with Dolutegravir Use:

The use of dolutegravir (Tivicay) in pregnant patients has recently been contested due to studies showing neural tube defects in newborns. This adverse event in women of child-bearing age has been brought to international attention due to an ongoing study in Botswana. This study focused on women receiving dolutegravir or efavirenz either before pregnancy or during weeks 19-21 of pregnancy. During the study, 845 women started dolutegravir during pregnancy and 4593 women started efavirenz. In the group of women who started dolutegravir, there were 4 cases of neural tube defects from 426 infants born during the study (0.67%). There were no reports of neural tube defects in those who started efavirenz before pregnancy or who started either medication, dolutegravir or efavirenz, at weeks 19-21 of pregnancy. According to the study, dolutegravir use is of issue when exposed during conception rather than during pregnancy.[2]

Antiretroviral Therapy During Pregnancy: Updates in Dolutegravir (Tivicay) Use

Preferred Agents		
Preferred NRTI's (pick 1 combination): ○ Abacavir/lamivudine (Epzicom) ○ Tenofovir disoproxil fumarate/ emtricitabine (Truvada) ○ Tenofovir disoproxil fumarate (Viread) and lamivudine (Epivir)	+	**Preferred Agents (pick 1 agent):** **PIs:** ○ Atazanavir (Reyataz)/ ritonavir (Norvir) ○ Darunavir (Prezista)/ ritonavir (Norvir) **INSTIs** ○ Raltegravir (Isentress)
Alternative Agents		
Alternative NRTIs: ○ Zidovudine/lamivudine (Combivir) **Alternative PIs:** ○ Lopinavir/ritonavir (Kaletra) **Fixed Dose Tablet:** ○ Rilpivirine/tenofovir disoproxil fumarate/ emtricitabine (Complera)		**Alternative INSTIs:** ○ Dolutegravir (Tivicay) **Alternative NNRTIs:** ○ Efavirenz (Sustiva) ○ Rilpivirine (Edurant)

Due to the results of the study, the World Health Organization (WHO) released a statement cautioning the public about the use of dolutegravir during pregnancy and the issue was also discussed at the International AIDS Conference 2018 held in July. While patients and practitioners should be cautious, the risk of neural tube defects is low and toxicology studies conducted by the manufacturer have shown no evidence of adverse events in animal studies. The international consensus on the issue is to adequately counsel women of childbearing age about the risks associated with dolutegravir and about the use of appropriate contraceptive methods before starting therapy. Women who would like to start therapy with dolutegravir are recommended to obtain a pregnancy test before initiation to avoid any potential adverse events. Women who are planning to become pregnant are encouraged to discuss alternative therapy options with their providers. Pregnancy data should be reported to the Antiretroviral Pregnancy Registry at www.apregistry.com.[1,3]

With the ongoing changes, the DHHS released updated guidelines in October 2018 for adults and adolescents containing recommendations from the WHO and providing information on the current controversies of treatment with dolutegravir. These guidelines have also listed precautions to take regarding initiation of dolutegravir in women of childbearing age. The Perinatal guidelines are currently undergoing changes to reflect those that have been made in the aforementioned guidelines.

References:

1. AIDSinfo. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents (2018). https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-treatment-guidelines/0/ (accessed 2018 Nov 3)
2. Levin J. Dolutegravir/tenofovir/emtricitabine (DTG/TDF/FTC) started in pregnancy is as safe as efavirenz/tenofovir/emtricitabine (EFV/TDF/FTC) in nationwide birth outcomes surveillance in Botswana. Presented at 9th IAS Conference on HIV Science. Paris, France; 2017 Jul.
3. World Health Organization. Statement on DTG – Geneva 18 May 2018 (May 2018). http://www.who.int/medicines/publications/drugalerts/Statement_on_DTG_18May_2018final.pdf (accessed 2018 Nov 3)

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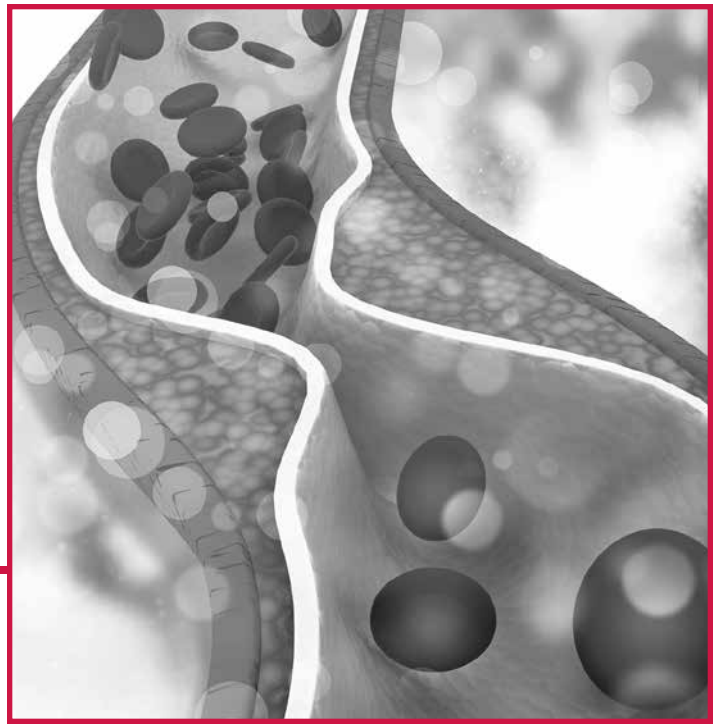
Clopidogrel use in Atherosclerotic Diseases

Atherosclerosis is the hardening and thickening of the walls of the arteries. This condition can occur as a result of build-up of fatty deposits on the inner lining of the arteries, calcification of the wall of the arteries or thickening of the muscular wall of the arteries from chronically high blood pressure, saturated fats, nicotine or elevated blood sugar levels (diabetes). The plaque builds up over a period of time and obstructs the normal flow of blood. Plaque causes blood to coagulate inside the artery and divest the organs of oxygenated blood. Ischemic events in the brain or heart can lead to stroke or myocardial infarctions.

Clopidogrel, marketed under the brand name Plavix(R), is an anti-platelet agent that has been approved by the FDA for prevention of atherosclerotic events, such as ischemic stroke and in-stent thrombosis. The clinical safety and efficacy of clopidogrel were shown in the Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) study. However, clopidogrel carries the risk of hemorrhage and also has some downsides which include its slow onset of action, non-reversible platelet binding, and interactions with other commonly administered drugs.

Clopidogrel inhibits ADP-induced platelet aggregation by direct inhibition of adenosine diphosphate (ADP) binding to its receptor and of the subsequent ADP- mediated activation of the glycoprotein GPIIb/IIIa complex. Many of the drugs that inhibit platelet function have been shown to reduce events that causes death in people with established coronary artery disease (CAD) as evidenced by stroke or transient ischemic attacks, myocardial infarction, unstable angina or the need for vascular bypass or angioplasty. This shows that platelets play a significant role in the initiation of these events and that inhibiting its function can reduce the rate of these events.

Clopidogrel is a prodrug that must be metabolized by CYP 450 enzymes, CYP2C19 to be precise in order to produce its active metabolite that prevents platelet aggregation. Although routine testing is not recommended, however, genetic testing prior to taking clopidogrel may be considered to identify poor metabolizers. Poor metabolizers taking clopidogrel at recommended doses will metabolize the drug less, therefore, a reduced effect on platelet inhibition. The active metabolite of clopidogrel selectively prevents the binding of adenosine diphosphate (ADP) to its platelet P2Y12 receptor and the subsequent ADP mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting irreversible platelet aggregation.



Clopidogrel comes in 75mg and 300mg tablets. There are no dosage adjustments necessary for both renal and hepatic impairments. It can be taken without regards to meals, however, avoidance or minimization of grape fruit or

grapefruit juice is highly recommended. At steady state, the average inhibition level seen with a dose of 75mg per day was between 40% and 60%. Other side effects include rash, diarrhea, tachycardia and stomach discomfort etc…

Due to the favorable benefit/risk ratio, clopidogrel has shown a clinically important advance in the treatment of patients with manifest atherosclerotic disease.

References:

1. CAPRIE Steering Committee. A randomized, blinded, trial of clopidogrel versus aspirin in patients at risk of ischemic events (CAPRIE). Lancet 1996; 348:1329-39.
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3. Clopidogrel. In: Lexi-Drugs Online Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: https://online-lexi-com.libaccess.fdu.edu/lco/action/doc/retrieve/docid/patch_f/6645#f_uses. Accessed September 27, 2018.

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Checkpoint Inhibitors

Checkpoint inhibitors are immunomodulatory antibodies that enhance the immune system. Programmed death-1 receptor (PD-1), PD-1 ligand (PDL-1), and antigen-specific CD8(+) T cells play an important role in the ability of cancer cells to invade host's immune cells. Cancer tissue has shown to limit host response through the upregulation of PDL-1 and its binding to PD-1 on antigen-specific CD8(+) T cells. This is called adaptive immune resistance. The interaction between PD-1 and PD-L1 directly inhibits apoptosis of the tumor cell, promotes peripheral T effector cell exhaustion, and promotes conversion of T effector cells to Treg cells. PD-L1 overexpression is related to a poor prognosis for several types of tumors, including renal-cell carcinoma, bladder cancer,
esophageal cancer, pancreatic cancer, gastric cancer, hepatocellular carcinoma, and ovarian cancer.

Treatment with PD-1 blockade agents results in an accumulation of functional T cells, which translates into tumor regression. By blocking the interactions between PD-1 and PD-L1, immune function is
enhanced and antitumor activity is mediated.

In 2014, antibodies that specifically block PD-1 were approved for melanoma and in 2015 for non-small-cell lung cancer (NSCLC) in the United States. Since a PD-1 blockade targets lymphocytes rather than cancer cells, it has a long-term therapeutic effect that persists even when cancers cause mutations.

Of the agents currently on the market, nivolumab and pembrolizumab target PD-1, while atezolizumab, avelumab, and durvalumab, target PD-L[1]. These immunomodulatory antibodies have been approved in various indications such as melanoma, renal cell carcinoma, non-small cell lung cancer, head and neck cancer, urothelial carcinoma, Hodgkin lymphoma, Merkel cell carcinoma, as well as microsatellite instability-high or mismatch repair deficient [dMMR] solid tumors.

Although there are many clinical benefits seen with these agents, checkpoint inhibition is associated with dermatologic, gastrointestinal, hepatic, endocrine, and other less common inflammatory immune related adverse events. These adverse events arise due to the immunological enhancement mechanism of action. The median time to onset of the adverse events differs depending on the type of toxicity, and can be roughly classified as early (<2 months: skin, gastrointestinal, or hepatic) or late (>2 months: pulmonary, endocrine, and renal-related). These side effects can be managed with temporary immunosuppression agents such as corticosteroids, TNF alpha antagonists, and mycophenolate mofetil.

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Checkpoint Inhibitors

(Continued from page 5)

As we can see, the PD-1 blockade is effective against many types of tumors because it enhances the anti-tumor activity of cytotoxic T lymphocytes (CTLs), which recognize various tumor-specific antigens. Although there are many adverse reactions associated with these agents, they can easily be managed and the benefits of using these agents outweigh the risks.

Citations:

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Steven-Johnson Syndrome (SJS)

Steven-Johnson Syndrome (SJS) is a rare but serious dermatological condition that can affect the skin and the mucous membranes. Toxic epidermal necrolysis (TEN) or Lyell's syndrome is a severe form of SJS. SJS and TEN are delayed-type hypersensitivity reactions that are mainly caused by medications. Degree of skin detachment can define whether it's SJS or TEN. In case of SJS, <10% of skin Is involved. Whereas, in case of TEN, >30% of skin is involved. SJS/TEN overlap when 10-30% of the skin is involved. The most common symptoms are skin-related symptoms. SJS can cause skin to turn purple or red and peel away. It can also cause painful cutaneous and mucous membrane (ocular, oral, and genital) lesions, and other systemic symptoms. Moreover, esophageal, nasopharyngeal, and genital mucosal involvement with blisters, erosions, and secondary development of strictures can occur.

SJS/TEN is more prevalent in women, HIV-infected people, and elderly. SJS/TEN represent as true medical emergency, it could be fatal if early recognition and appropriate management is not provided. Initially, there are non-specific symptoms: stinging of the eyes, discomfort with swallowing, influenza-like illness (fever, cough, malaise), and joint pain. Followed by: bruises with blisters on top; patches of red and painful skin, blisters on the face, palms of hands, soles of feet, or chest. Moreover, there can be swelling, sores, crusting on moist, pink skin that lines the eye, mouth, lungs, genitals and other areas, which can lead to red and watery eyes, trouble urinating, trouble breathing, or lung infection.

SJS/TEN can be caused by infections such as HIV, Mycoplasma pneumoniae, Hepatitis virus, and Herpes virus. Moreover, the cause could be malignancies or idiopathic. However, the majority of the cases are caused by medications. Following medications can cause SJS/TEN:

Among these medications, the most high-risk drugs that can cause SJS/TEN are: allopurinol, anti-epileptic drugs, anti-infective sulfonamides, chlormezanone, nevirapine, and non-steroidal anti-inflammatory drugs of the -oxicam type. In addition, new biologicals and herbal remedies can also be considered causative agents.

sulfonamides	fluoroquinolones	macrolides	metronidazole	cephalosporins
aminopenicillins	tetracyclines	phenobarbital	sodium valproate	levetiracetam
phenytoin	lamotrigine	carbamazepine	oxcarbazepine	carbamate
furosemide	acetazolamide	diclofenac	ibuprofen	rofecoxib
mirtazapine	duloxetine	allopurinol	aspirin	acetaminophen
imatinib	sunitinib	afatinib	vandetanib	dipyridamole
danazol	androgen anabolic steroids	paclitaxel	docetaxel	tegafur/ gimeracil/ uracil
oseltamivir	adefovir	nevirapine	thalidomide	lenalidomide
Ramipril	strontium ranelate	lopentol	fexofenadine	mizoribine
glipizide				

Septicemia, also known as bacteremia or blood poisoning, is a serious bloodstream infection. It is the leading cause of morbidity and fatality in the acute phase of SJS/TEN. A multidisciplinary approach is needed for the acute management of SJS/TEN. It is mandatory to immediately withdraw the drugs that caused SJS/TEN, because the first step of treating SJS/TEN is to eliminate any causative factor. Next step is to promptly provide specific supportive treatment, which includes parenteral or nasogastric feeding and administration of intravenous fluids. Patient should be checked for any signs of infection, because people with SJS/TEN can develop serious infections. In case of an infection, antibiotics can be given to treat the infection. The final step is to provide symptomatic treatment to the patient. Try to keep the skin clean and healthy, which might involve keeping it moist, adding dressings, and gently removing dead skin etc. Medicine to help reduce the pain in the skin can be given to patient as well. In most cases, cyclosporine A, immunoglobulins, and systemic corticosteroids are used for the treatment of SJS/TEN. Cyclosporine is used to help slow down the symptoms. Prednisone can be used to reduce inflammation. Increased mortality is associated with other potential therapeutic measures like cyclophosphamide, thalidomide, and TNF-alpha inhibitor.

SJS/TEN are adverse hypersensitivity reaction that can be life threatening in most cases. It is important to understand the proper cause of SJS/TEN in order to provide proper treatment. Earlier diagnosis and management of SJS/TEN results in better treatment outcome.

References:

1. Steven-Johnson Syndrome and Toxic Epidermal Necrolysis (Patient Education – Disease and Procedure). Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://online.lexi.com. Accessed September 11, 2018.
2. Fakoya AOJ, Omenyi P, Anthony P, et al. Stevens - Johnson Syndrome and Toxic Epidermal Necrolysis; Extensive Review of Reports of Drug-Induced Etiologies, and Possible Therapeutic Modalities. Open Access Macedonian Journal of Medical Sciences. 2018;6(4):730-738. doi:10.3889/oamjms.2018.148.
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Acetaminophen for Patent Ductus Arteriosus (PDA) Treatment of Neonatal ICU

In medicine, the word "patent" means open, unobstructed, or not closed. PDA is a condition in which the ductus arteriosus does not close. The ductus arteriosus (DA) is a blood vessel that serves as an imperative vascular linkage between the main pulmonary artery and aorta. Its purpose is to divert blood flow in order for the blood to bypass a baby's lungs during fetal life. Once the baby is born and its lungs are filled with air, the DA actively constricts until it is eventually obliterated since it is no longer needed. If this vessel fails to close completely after delivery, it is referred to as a PDA.

PDA is most common in premature infants, especially in those with a very low birth weight, respiratory destress syndrome or congenital heart problems such as pulmonary stenosis or hypoplastic left heart syndrome. If a PDA stays open, a baby is more prone to develop complications such as heart failure, elevated blood pressure, or an infection of the inner lining of the heart.

One of the treatment approaches of a PDA in preterm infants includes pharmacologic closure of the DA. This is often done by using non-selective cyclooxygenase (COX) inhibitors such as indomethacin and some data exists using ibuprofen. Limited case series explored the use of acetaminophen for this indication. When using ibuprofen for PDA closure, the standard dosing consists of an initial 10 mg/kg dose followed by two subsequent 5 mg/kg doses given at 24-hour intervals. Indomethacin is given intravenously as multiple 0.1-0.2 mg/kg doses administered at 12- to 24-hour intervals. However, these two agents have complication risks, including but not limited to NEC (necrotizing enterocolitis).

In a prospective study consisting of 300 preterm infants with a gestational age of less than 28 weeks, less than 1500 gm in the first 2 weeks of life with PDA diagnose, the patients were randomly assigned (with each group having an N=100)IV paracetamol (acetaminophen), IV ibuprofen, or IV indomethacin. All three of these agents showed the same effect regarding PDA closure, but there were less adverse effects in the paracetamol group. The infants in the ibuprofen and indomethacin groups experienced adverse effects including elevations in blood urea nitrogen and serum creatinine.

Results of an observational study done at the University of Padua also showed evidence favoring the use of acetaminophen for PDA closure in selected preterm infants. Intravenous administration of acetaminophen was shown to be equally effective to the FDA approved therapy. There might be a role for acetaminophen for the treatment of PDA in patients who fail ibuprofen or have contraindications.

In order to properly determine the safety and efficacy of IV acetaminophen for PDA closure in preterm infants, further investigations, such as randomized control trails, are warranted and more conclusive data is needed. Currently, acetaminophen IV for PDA in infants is not FDA approved.

References:

1. El-Mashad AE, El-Mahdy H, El Amrousy D, Elgendy M. Comparative study of the efficacy and safety of paracetamol, ibuprofen, and indomethacin in closure of patent ductus arteriosus in preterm neonates. Eur J Pediatr 2017; 176:233.
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3. Valerio E, Valente MR, Salvadori S, et al. Intravenous paracetamol for PDA closure in the preterm: a single-center experience. Eur J Pediatr 2016; 175:953.
4. Webb GD, Smallhorn JF, Therrien J, Redington AN. Congenital heart disease. In: Mann DL, Zipes DP, Libby P, Bonow RO, Braunwald E, eds. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 10th ed. Philadelphia, PA: Elsevier Saunders; 2015:chap 62

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Valsartan Recall: Ongoing Process

On July 13, the Food and Drug Administration (FDA) announced a voluntary recall of products containing the active ingredient of valsartan. Valsartan, an angiotensin II receptor blocker (ARB), is one of the most commonly prescribed high blood pressure and heart failure medications. European Union (EU) announced the valsartan recall on July 5th, before the FDA made an announcement on July 13th.1 The recall involves about 2,300 batches that were sent to many countries around the world.[1]

The reason for the recall is that trace, but unacceptable amounts of potent carcinogen N-nitrosodimethylamine (NMDA) were detected in the API, manufactured by Zhejiang Huahai Pharmaceuticals, in Linhai, China1. This contaminated API was used by manufacturers such as Solco HealthCare, Camber Pharmaceutical, Teva Pharmaceuticals, Major Pharmaceuticals, and Torrent Pharmaceutical.2 Exposure to high levels of NMDA may cause liver damage in humans.3. It is believed that NMDA is related to changes in the way the active substance was manufactured. Also, some levels of impurity may have been in the valsartan containing products as long as four years. Known as an environmental contaminant, NMDA can also be exposed to humans via water, meats, dairy products, and vegetables. [2]

Although many products containing valsartan are being recalled, not all products are being recalled. However there are ongoing investigations and constant updates on additional products being recalled. Therefore, it is important for valsartan prescribers to stay updated with list of valsartan products that are and are not under recall. A list of recalled valsartan products can be found on FDA website (www.fda.gov).

Physicians should note that valsartan is a Non-Formulary drug at University Hospital and the hospital utilizes losartan instead. Therefore the hospital does not have the impacted valsartan product in the pharmacy stock. Although it has potential danger, the FDA determined that the recalled valsartan products pose an unnecessary risk to patients. Therefore, the FDA recommends patients use safe valsartan containing medicine listed by FDA or consider other treatment options. Physicians should quarantine and stop distributing the affected products.

It is important that patients should continue to take their current medication until the prescribing doctor or pharmacist gives him/her a replacement or different treatment options. If a patient is taking valsartan containing medication, he/she should compare the company, National Drug Code, and lot number on his/her prescription bottle with the information in the list provided by the FDA. Another option is that patient can bring the medication bottle to the local pharmacy and ask the pharmacist. If a patient has the recalled medicine, patient should contact his/her pharmacist and the pharmacist may be able to provide the patient with valsartan made by another company unaffected by the recall. If it is not possible to get an unaffected product, the patient should contact the prescribing doctor and discuss other treatment options.[2]

Consumers and health care professionals should report any adverse reactions with valsartan containing products, to the FDA's MedWatch program to help the agency better understand the scope of the problem. Potential symptoms of overexposure include headache, fever, nausea, jaundice, vomiting, abdominal cramps, enlarged liver, reduced function of liver, kidneys and lungs and dizziness3. Go to www.fda.gov/medwatch/report.htm and report online or download and complete the appropriate form, then submit it via fax at 1-800-FDA-0178

(Continued on page 10

Valsartan recall: ongoing process

(Continued from page 9)

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1. Christensen, J. (2018, July 06). Common heart drug recalled in 22 countries for possible cancer link. Retrieved August 20, 2018, from https://www.cnn.com/2018/07/06/health/valsartan-heart-drug-recall-intl/index.html
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Metabolic Comorbidities in Patients with Mental Illness

A common diagnosis in the United States is obesity which goes hand in hand with many other comorbidities such as diabetes, hyperlipidemia, and hypertension, is also seen within the mentally ill population. A large number of mentally ill people do not have the cognitive capabilities to take care of themselves. Many patients with mental illness are part of an underserved population, which puts many of these patients at risk for homelessness and poor healthcare. With limited access to healthy food, shelter, and necessary medications, many patients go untreated and are prone to develop additional comorbidities.Their lack of access to attain the necessary medical attention and proper medication access and management creates a pitfall for the mentally ill patient.

Compounded by poor life circumstances and reduced access to medical care, antiphycotic medications can induce or exacerbate metabolic comorbidities. Studies show that once patients are stable on a treatment regimen even switching them to monotherapy on a different medication can cause an increase in symptoms due to metabolic imbalance. It is important for patients to continue using the regimen that keeps them stable. It has been known for some time that patients with serious mental illnesses tend to have a shorter life expectancy than their peers in the community who do not have the same conditions. According to Ganguli, "This life-expectancy gap has been reported to be as much as 25% shorter which is commonly due to cardiovascular (CV) disease." People with mental illnesses often have high-risk lifestyle conditions and antipsychotic-induced CV side effects which leaves them more susceptible to developing metabolic syndrome.

Interdisciplinary collaboration by the healthcare personnel is vital when treating mental illness along with highlighting methods by which the patients can modify their lifestyle as an adjunct to their medication regimen. A common side effect of antipsychotic medications is sedation which poses as a barrier to exercising. Providing alternative recommendations of medications which have a lower risk of causing sedation would help patients remain more active. A study done by Vancampfort shows the importance of interventions promoting the walking capacity in people with bipolar disorder, particularly in patients at a high risk for cardiovascular diseases due to developed comorbidities.

Having more resources available to help these patients remain adherent to treatment plans and follow non-pharmacological lifestyle changes may lead to a decrease in the occurrence of metabolic comorbidities in patients with serious mental illness.

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2012 CHEST Guideline on Antithrombotic Therapy in Atrial Fibrillation Updated After Six Years

On August 22, 2018, the American College of Chest Physicians® (CHEST) published their first updated version of the ninth edition of the antithrombotic therapy guideline for patients with atrial fibrillation (AF).[1,2] AF affects over two million adults in the United States, posing a major public health burden.[3] The incidence of AF increases with advanced age and cardiac conditions such as congestive heart failure.[3] As ectopic foci signals originate in the atrial tissue during AF, hemostasis can occur in the left atrium during diastole, which can lead to thrombus formation and ultimately ischemic stroke.[3,4] Stroke is one of the most common and life-threatening complications of AF.[3,4] Therefore, preventing and treating stroke complications of AF with antithrombotic therapy is of paramount importance.[4,5]

These updates take into account the findings of the most current clinical research on this topic since the publication of the previous version in 2012. Although the new guideline provides a total of sixty graded recommendations, only six remain unchanged from the last version.[2] The focus of the guideline is on stroke prevention and its integration into a holistic approach to manage AF.[2] As such, the treatment recommendations fall into three domains: stroke and bleeding risk assessment, antithrombotic therapy in general, and antithrombotic therapy in special situations.[2]

The following are key differences between the previous and latest renditions of the guideline:

2012 Guideline[1]	**2018 Guideline[2]**
• Provides recommendations based on high/intermediate/low risk stratification using the $CHADS_2$ schema	• Recommends assessing stroke risk using a risk factor-based approach and the CHA_2DS_2-VASc schema
• Does not directly recommend clinicians to make bleeding risk assessment	• Recommends the use of the HAS-BLED scoring system to perform bleeding risk assessment at every patient encounter and to address modifiable bleeding risk factors
• Suggests no therapy rather than antithrombotic therapy for AF patients at low risk of stroke (e.g., $CHADS_2$ score of 0) • Gave a grade 2B recommendation to use aspirin (75 mg to 325 mg once daily) for low risk patients who do opt to receive antithrombotic therapy	• Recommends against antithrombotic therapy in AF patients at a low risk for stroke as identified using the CHA_2DS_2-VASc score (0 in males or 1 in female)

Abbreviations:

- CHADS2 = congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischemic attack (doubled)
- CHA2DS2-VASc = congestive heart failure [or left ventricular systolic dysfunction], hypertension, age ≥ 75 years (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65 to 74 years, sex category (female)
- HAS-BLED = hypertension, abnormal renal/liver function (1 point each), stroke, bleeding history or predisposition, labile INR, elderly (> 65 years), drugs/alcohol concomitantly (1 point each)

Moreover, the updated guideline provided recommendations on the controversial topic of triple antithrombotic therapy in AF patients with concomitant acute coronary syndrome status post intracoronary stent (bare metal or drug eluting) placement. While the 2012 guideline provided recommendations either for

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or against triple antithrombotic therapy on the basis of stroke risk using the CHADS2 schema and time period after intracoronary stent placement, the 2018 guideline further took into account the level of bleeding risk using the HAS-BLED schema.[1,2]

Furthermore, the 2012 guideline suggested using dabigatran 150 mg twice daily in lieu of an adjusted-dose vitamin K antagonist (VKA) such as warfarin in AF patients who qualify for oral anticoagulation therapy.[1] However, since 2012, more data has been published surrounding the effectiveness and safety of the then-new, direct-acting oral anticoagulant (DOAC) drugs such as apixaban, rivaroxaban, and edoxaban in AF. As such, the updated guideline expanded their recommendations to include these options for patients who qualify for oral anticoagulant therapy.[2]

Other areas that are worth examining in the updated guideline include recommendations on when to switch patients on a VKA to a DOAC, importance of time in therapeutic INR window if using a VKA, and anticoagulant therapy considerations in pregnancy and lactation to name a few.[2]

Consistent with CHEST's "living guidelines" model, the 2018 version builds upon the last update as new evidence has become available. This will aid clinicians in providing evidence-based and quality patient care, especially given the rising incidence, prevalence, and burden of atrial fibrillation.

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Welcome to Two New Pharmacists

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Recent graduate from Rutgers Pharmacy, Chrystel's excited to be a part of a team that promotes learning and teamwork. She even convinced her sister to join pharmacy school. She likes reading mystery novels, and is a huge fan of Harry Potter and Sherlock Holmes; she recently started reading House of Silk.