UFHealth
SHANDS HOSPITAL

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Drugs & Therapy BULLETIN

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met October 15, 2013. 1 product was added in the *Formulary,* 3 drugs were designated non-formulary and not available, 1 product was designated high-priority non-formulary, and 1 therapeutic interchange was approved. Criteria for use was added for 1 agent.

◆ ADDED

Del Nido Cardioplegia Solution
(compounded product)

◆ NON-FORMULARY AND NOT AVAILABLE

Albuterol/Ipratropium Inhaler
(Combivent Respimat®)*
**Patient may use their own*

Brimonidine Topical Gel 0.33%
(Mirvaso®)*
**Patient may use their own if provided in sealed, original container*

Topiramate Extended Release
(Trokendi XR®)§
§Therapeutic Interchange

◆ HIGH-PRIORITY NON-FORMULARY

Mechlorethamine Gel
(Valchlor®)

◆ CRITERIA FOR USE CHANGE

Tromethamine (THAM®)*
**Restricted to severe metabolic acidosis associated with hypernatremia*

Del Nido Cardioplegia Solution is a cardioplegic solution utilized during heart surgeries. When surgeries are performed directly on the heart, it is often necessary to temporarily arrest the heart in order to still its movement, decrease oxygen demand, and preserve tissue function. This, in conjunction with aortic cross-clamping can provide a still, bloodless field

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DRUG POLICY

Patient's Own Medication in the Inpatient Setting

In most instances, medications administered to patients admitted to the hospital are provided by the Pharmacy Department. However, there may be circumstances where patients are allowed to bring their own medications into the facility for use while hospitalized. These situations are generally kept at a minimum secondary to medication safety concerns.

In a report by the Pennsylvania Patient Safety Advisory, a number of medication errors with patient's own medications are described.[1] Between July 1, 2004 and January 31, 2011, 879 medication errors were reported with 77% reaching the patient and 2% classified as causing patient harm. In addition, a number of these errors note that medications have been found in the patient's room without hospital staff being aware. The most commonly identified errors were: Unauthorized Drug (48%), Extra Dose (8%), Wrong Dose/Overdose (2.3%), Monitoring Error (1.8%), Wrong Drug (1.7%) and Other (23.1%). In addition to safety concerns, there are also concerns regarding drug security.

The Joint Commission addresses patient's own medication use in standard MM.03.01.05 which reads "The hospital safely controls medications brought into the hospital by patients, their families, or licensed independent practitioners."[2] In order to comply with this standard, the hospital must address the following elements:

- Define when medications brought into the hospital by patients can be administered and inform patient or family when patient's own medication is not permitted.
- Identify the medication and visually inspect the medication for integrity.

In order to address both the medication safety and security concerns, UF Health – Shands Hospital maintains a Core Policy (#CP02.077) detailing the procedures for patient's own medication use at our facility.

In February 2013, the Patient's Own Medication Policy was updated to reflect current best practices. When medications are brought into the hospital by the patient, the medication should be sent home with a caregiver when possible. If there is no mechanism by which this can occur, the medication will be stored as a patient valuable with Security. If the medication is non-formulary and there is no available alternative in the *Formulary*, the patient may use their own medication when the following conditions are met:

- The prescriber enters a complete order in EPIC including name, dose, route, frequency, and instructions for use.
- The order indicates that patient may take his/her own supply.
- The product is stored in its original container or prescription vial and must be identified by the pharmacist prior to administration.
- Nutritional supplements and/or alternative medications may only be used if they are in an original, sealed container.

Once the above have been confirmed, the patient will be allowed to utilize their own medication. These medications will be housed in the Omnicell cabinet and administered by a healthcare professional in line with current medication administration practice.

There are certain instances where patients will never be allowed to utilize their own medication. If a medication is currently listed in the *Formulary*, patients will be unable to utilize their own medication and should use hospital supply. Patients are not allowed to take their own controlled substances, oral liquids, or open topical medications. In

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Formulary update, *from page 1*

that will allow for increased surgical precision during cardiopulmonary bypass. Cardioplegia solutions are used to induce cardiac arrest and prohibit cardiac movement after aortic cross-clamping has been performed.

Currently, UF Health – Shands Hospital utilizes a microplegia solution that is prepared in-house. When the standard microplegia is used, it requires re-administration to the coronaries approximately every 15 minutes to maintain a state of arrest. Additionally, the perfusionist's cannulas must remain in the surgical field when delivering microplegia secondary to the frequent administrations. This results in frequent interruptions and impaired visualization of the surgical field.

The newly added Del Nido Solution can maintain a state of arrest for approximately 1-3 hours with a single dose. This allows for single administration as well as removal of the cannula resulting in cardiac arrest while maintaining an adequate visual field.

The base formulation for the Del Nido Cardioplegia Solution is Plasma-Lyte A to which mannitol, magnesium sulfate, sodium bicarbonate, potassium chloride, and lidocaine are added. This crystalloid solution is then mixed with blood in a ratio of four parts solution to one part fully oxygenated whole blood, obtained from the bypass circuit. The Del Nido crystalloid solution differs from other cardioplegia solutions by eliminating the addition of calcium. However, the final mixed cardioplegia will contain trace amounts of calcium, due to the 20% composition of the patient's whole blood.

Del Nido Cardioplegia Solution could be compounded in-house, or procured from a compounding pharmacy. Preparation in-house would yield a limited beyond use date which would require patient-specific doses to be compounded as needed with a rapid turn-around time. In order to eliminate this emergent need for preparation of the solution, compounding pharmacies are currently being investigated for provision of the solution. Use of a compounding pharmacy would allow beyond use dating of 14 days under refrigeration.

Del Nido Cardioplegia Solution was added in the *Formulary* pending identification of a suitable vendor for purchase. This vendor must comply with all stipulations as set forth in the Compounding Pharmacy Policy #13-03-007.

Albuterol/Ipratropium Inhaler is a combination bronchodilator which is FDA-approved for use in adult patients with chronic obstructive pulmonary disease. Due to the chlorofluorocarbons (CFCs) contained in the original aerosol product, the inhaler version of Combivent® has been removed from the market. Combivent Respimat® contains the same ingredients as the original inhaler, yet does not contain CFCs. This agent cannot be utilized in ventilated patients and requires manual dexterity to administer. For this, and other financial reasons, the P&T Committee designated this agent Non-Formulary and Not Available in June 2013. Patients requiring Combivent Respimat® therapy would instead be administered nebulized ipratropium and albuterol (Duonebs®).

The Pediatric Emergency Department petitioned the Committee to re-evaluate the NFNA status of this product. Rationale for re-evaluation was a reduction in cardiovascular effects of albuterol when administered via inhaler vs. nebulizer, as well as pre-school children have been shown to have greater efficacy in the inhaler plus chamber with a mask versus nebulization with albuterol inhalers. Nebulization also requires a 15 min administration vs. 1-2 minutes for inhaler.

An independent evaluation of the literature supporting use of inhalers vs. nebulizers was performed. There is evidence to suggest that monotherapy with beta agonists delivered via MDIs is superior to monotherapy delivered via nebulizers in children with acute asthma in regards to hospital admission and adverse effects. However, this data does not exist for ipratropium inhalers or for Combivent Respimat® inhalers. Additional data suggests combination therapy with a beta agonist and anticholinergic is superior to beta agonist monotherapy in this population although it is not specific to Combivent Respimat® In discussions with Respiratory Therapy, there was a lack of comfort in utilizing the Combivent Respimat® inhalers with an AeroChamber.

Since that discussion, abstract data has been presented which discussed Combivent Respimat® with AeroChamber devices. These discussed appropriate handling of the device and inhalation volume, detailing the amount of drug delivered via inhalation. Although not specifically discussed, extrapolation of this data indicates that efficacy when used in this manner is likely. With this data, use of Combivent Respimat® through an AeroChamber (1 inhaler for several patients) was proposed. This is thought to carry minimal risk of cross-contamination as the AeroChamber has a one-way inhalation and one-way exhalation valve. This is similar to what is already being performed in the pulmonary function test lab. A new AeroChamber would be used for each patient. Infection Prevention and Control was contacted regarding this practice and agreed the risk of contamination between patients is low. However, respiratory therapy has pointed out that although a new chamber would be used, there is no way to clean the actual inhaler itself in between patients as you cannot remove the cartridge once it is inserted. From a procedural standpoint, this is different than any other inhaler product and would therefore create different standards of practice, which may lead to medication errors with other inhaler devices.

Overall, the benefit of the Combivent Respimat® product in pediatric patients with asthma has not been demonstrated. There is evidence to support to the use of albuterol inhalers over nebulizers which are currently available in the *Formulary* and stocked in the pediatric ED. Utilization of the albuterol inhaler in conjunction with nebulized ipratropium may be an appropriate therapeutic option. After discussion, the Committee determined that at this time, there is not enough evidence to support the addition of Combivent Respimat® in the *Formulary*. While they agreed there is evidence with the albuterol MDI, they did not feel strongly that that addition of ipratropium was necessary in a MDI form vs. nebulizer. The product will remain Non-Formulary and Not Available.

Brimonidine 0.33% Topical Gel (Mirvaso®) is an alpha adrenergic agonist indicated for the treatment of persistent (non-transient) facial erythema of rosacea in adults aged 18 years or older. This is not typically an inpatient issue and therefore the Committee recommended this agent be designated Non-Formulary and Not Available. Patients would be able to utilize their own medication provided that it is a sealed product which is brought in the original container as per the Patient's Own Medication Core Policy.

Topiramate Extended Release (Trokendi XR®) is an anti-epileptic agent indicated for the treatment of partial onset and primary generalized tonic-clonic seizures in addition to Lennox-Gastout Syndrome in patients 6 years of age or greater. It is available as extended release capsules containing 25 mg, 50 mg, 100 mg or 200 mg.

Results of a pharmacokinetic study evaluating XR vs. IR formulation (same total daily dose) indicate that Cmax and AUC for multiple time points are within bioequivalent limits which indicated no clinically significant difference between the formulations.

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Formulary update, *from page 2*

A one-to-one daily dose therapeutic interchange was approved as follows:

Topiramate Immediate Release (Topamax®)	**Topiramate XR** (Trokendi XR®)
25 mg PO BID	50 mg PO Daily
50 mg PO BID	100 mg PO Daily
100 mg PO BID	200 mg PO Daily
200 mg PO BID	400 mg PO Daily

Mechlorethamine Gel (Valchlor®) is an alkylating agent indicated for the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have received prior skin-directed therapy. Individuals other than the patient must avoid skin contact with the agent and there is a risk of embryo-fetal toxicity. This is also an alcohol-based gel and therefore, is flammable. This agent will be added in the Chemotherapy Policy.

The Formulary Subcommittee recommended that this product be viewed as a line item extension of mechlorethamine IV which was removed from the *Formulary* in January 2013. This product will carry the same designation of High-Priority Non-Formulary.

Tromethamine Injection (THAM®) is an organic amine proton-acceptor which allows it to integrate as a component of the body's buffering system upon intravenous administration. Tromethamine combines with hydrogen ions which are then excreted in the urine. It is FDA-approved for alkalization during cardiopulmonary bypass and correction of metabolic acidosis during both cardiopulmonary bypass operations and cardiac arrest.

After being without any supply of THAM® for approximately 18 months, we have recently obtained a supply of the product and have proposed restricted use. Review of the article "Severe Metabolic or Mixed Acidemia on Intensive Care Unit Admission: Incidence, Prognosis, and Administration of Buffer Therapy: A Prospective, Multiple-Center Study" by Jung and colleagues assisted with the development of the following criteria for use:

Severe metabolic acidosis associated with hypernatremia: Where relevant definitions / lab parameter requirements to facilitate operationalizing this restriction include all of the following:

Arterial pH < 7.2

Arterial Bicarbonate < 18 mEq/L

Serum Sodium > 150 mmol/L

NEWS

Fearing the Fluoroquinolones

On August 15, 2013, the U.S. Food and Drug Administration (FDA) issued an official Safety Communication requiring changes to labeling and Medication Guides for all systemic formulations (oral and intravenous) of fluoroquinolones to include a warning of possible permanent nerve damage.[1] The updates will include the serious adverse effect of peripheral neuropathy which can potentially occur shortly after the drug administration. This is an update to the existing labeling mandated by the FDA in 2004 with an emphasis on the rapidity and possible permanence of developing nerve damage.

This warning applies to ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, and ofloxacin. Topical formulations (otic and ophthalmic) are not known to be associated with this risk. Symptoms of nerve damage include pain, burning, tingling, numbness, weakness, or changes in sensation to light touch, pain or temperature, or body position.[1] If a patient develops these symptoms, the fluoroquinolone should be discontinued, and alternative therapy with a different class of antibiotic should be initiated unless a benefit to risk analysis warrants continuation of therapy.[1]

This new warning adds to the myriad of adverse effects already observed within the fluoroquinolone class. A recent study published evaluating oral ciprofloxacin, levofloxacin, and moxifloxacin in individuals with diabetes, identified a profound risk of hypoglycemia associated with moxifloxacin utilization.[2] This is not surprising as disruptions in glucose metabolism led to gatifloxacin's withdrawal from the market in 2006. A study published in the New England Journal of Medicine concluded that gatifloxacin, when used in the geriatric population in outpatient settings, resulted in inpatient admissions for management of dysglycemic events.[3,4]

Currently, all fluoroquinolones carry boxed warnings for tendinitis/tendon rupture and myasthenia gravis. Agents with increased anaerobic activity, such as moxifloxacin, have also been implicated in the development of *Clostridium difficile* infections. Other adverse effects involve cardiac toxicities with QT interval prolongation, hepatic dysfunction with liver enzyme abnormalities, and dermatologic reactions in the form of systemic rashes. In addition to the numerous aforementioned adverse effects, there is a significant drug interaction whereby co-administration with aluminum- and magnesium-containing products decreases oral absorption of fluoroquinolones.

The increased risk of adverse events is concerning as these broad-spectrum agents are commonly prescribed for the treatment of pneumonia, urinary tract, and skin and soft tissue infections. Although, high rates of fluoroquinolone resistance have caused these agents to fall out of favor in most institutions. Antimicrobial stewardship programs must consider collateral damage, along with safety and efficacy within this class of antibiotics. Currently at UF Health – Shands Hospital ciprofloxacin is restricted to 72 hours of therapy unless it meets certain criteria for use beyond this timeframe. Moxifloxacin is restricted for the treatment of mycobacterial infections. It may be prudent to re-examine this policy and take a closer look at levofloxacin, which is currently unrestricted.

In conclusion, the fluoroquinolones are not benign drugs and numerous toxicities warrant a shift toward more cautious prescribing practices, specifically in certain populations such as the elderly and those with diabetes. As clinicians, it is our paramount responsibility to be better antimicrobial stewards to effectively preserve the integrity of antimicrobial agents for severe infections while minimizing adverse events.

–Trang Trinh, PharmD

References available upon request from the Editor.

Patient's Own Medication, *from page 1*

addition, the majority of patient's own injectable medications cannot be used while inpatient. Exceptions to the policy include: epoprostenol, treprostinil, insulin, or other similar infusions administered via patient's own infusion device, injectable medications contained in an implantable device (i.e. baclofen), restricted distribution injectable medications, and injectable clotting factors used in the treatment of hemophilia. Specifics regarding when it is appropriate to utilize a patient's own injectable are outlined in the Core Policy.

When in doubt, patients should not utilize home medications, but rather use those provided by the institution. In order to prevent medication errors and/or loss of medication, strict adherence to this practice is warranted. Questions may be answered by reading CP02.077 available on the UF Health Portal.

– Carrie Lagasse, PharmD, BCPS

References available upon request from the Editor.

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