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Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met November 16, 2004. 3 drugs were added in the *Formulary* and 2 drugs were deleted. 3 drugs were designated nonformulary and not available. 3 therapeutic interchanges were approved and restrictions were approved for 1 drug.

◆ ADDED

Cefoxitin
(Mefoxin® and generics)

Cilostazol (Pletal® by Otsuka American Pharmaceuticals)

Ciprofloxacin + Dexamethasone Otic Suspension
(CiproDex® by Alcon)

◆ DELETED

Cefotetan
(Cefotan® and generics)*

Codeine Liquid (generic)*

**Nonformulary and not available*

◆ NONFORMULARY AND NOT AVAILABLE

Ciprofloxacin + Hydrocortisone Otic Suspension
(Cipro® HC by Alcon)

◆ THERAPEUTIC INTERCHANGES

Cefoxitin for **Cefotetan**

Individual Ingredients for **Emtricitabine + Tenofovir (Truvada®)**

Pantoprazole IV for **Lansoprazole IV**

◆ RESTRICTIONS APPROVED

Fosphenytoin
(Cerebyx® by Parke Davis)

(continued on next page)

MEDICATION SAFETY

Banned abbreviation compliance

The Joint Commission for the Accreditation of Healthcare Organizations is emphasizing the medication safety concerns caused by common abbreviations. The Commission has mandated that these abbreviations no longer be used. Orders written using these abbreviations *(see table on page 4)* are considered invalid.

Regardless of the difficulty, compliance is a requirement, not an option.

Hospitals around the country have struggled with how to get prescribers to stop using abbreviations that have been used for years. Regardless of the difficulty, compliance is a requirement, not an option. Some hospitals require that every single order with a banned abbreviation be re-written. As you can imagine, this can be very time consuming. In some cases, the delay caused by these order clarifications could adversely affect patient care.

Despite many educational efforts to explain the risks of the banned abbreviations, their use has continued. Thus, education alone is not the answer.

Since holding orders could potentially harm patients and requires a massive amount of manpower, and since education works slowly and has limitations, how can we possibly solve this problem and avoid regulatory problems? Recently, Shands has entered into an agreement with the College of Medicine that provides financial incentives for improvement in quality measures (ie, Academic Quality Support Agreement or AQSA). Avoiding the use of the 10 banned abbreviations in the table is 1 of 84 quality indicators being monitored. Compliance with each quality indicator results in potential financial compensation to the College of Medicine. This provides positive incentive for change.

There is some initial indication that this approach is working. The first official audit of the use of banned abbreviations was done in September 2004. The bad news was that in an 8-hour period on 1 day, there were 229 banned abbreviations used. This means over 600 banned abbreviations were being used in 1 day! Clearly, contacting the prescriber for a new order for each of these 600 banned abbreviations would be impractical. However, trend data show some improvement and provides some insight as to where improvement efforts need to be focused.

In September, there was a 59% compliance rate (ie, number of avoided abbreviations divided by total number of opportunities to use one of the banned abbreviations). In October, the compliance rate rose to 69%. We are optimistic that this trend will continue. The AQSA target is 90%.

Of the 10 banned abbreviations, "cc," the ">" and "<" symbols, and "QD" are the most often abbreviations still used. The use of "units" instead of "U" has been the greatest improvement, and the use of this abbreviation is rarely noted.

One innovative method of writing orders about when to "Contact House Officer" is to create "less than" and greater than" columns, then list the monitoring variables as rows. This avoids spelling out "less than" or "greater than" for each monitoring variable. Another solution is to create standing orders.

Avoiding banned abbreviations is difficult. Old habits are hard to break. However, patient safety requires continued vigilance.

(See Table on Banned Abbreviations, page 4)

INSIDE THIS ISSUE

Formulary update, *from page 1*

Cefoxitin, a second-generation cephalosporin, was added in the *Formulary* when **cefotetan**, the current second-generation cephalosporin listed in the *Formulary*, was discontinued by its manufacturer.

Cefotetan orders will be automatically interchanged to cefoxitin. For surgical prophylaxis, cefoxitin will be interchanged on a milligram-for-milligram basis. However, because cefoxitin has a shorter half-life than cefotetan, cefoxitin will have to be given more frequently than cefotetan for moderate and severe infections. For moderate to severe infections when cefotetan 2 grams IV every 12 hours is prescribed, cefoxitin 2 grams IV every 6 hours will be dispensed. For severe infections when cefotetan 3 grams IV every 12 hours is prescribed, cefoxitin 2 grams IV every 4 hours will be dispensed. As with all therapeutic interchanges, a note will be placed in both the Orders and Progress Notes sections of the chart to alert the prescribers and nursing staff of this interchange.

Although cefotetan is still considered the preferable second-generation cephalosporin, its unavailability made this change necessary. Cefoxitin is available only in limited quantities. Therefore, it is recommended that its use be limited to pre- and peri-operative therapy. Cefazolin plus metronidazole is an alternative for intra-abdominal infections and gynecological surgeries. Metronidazole's anti-anaerobic activity will cover organisms like *Bacteroides fragilis*, which are covered by cefoxitin (and cefotetan).

Cilostazol is a phosphodiesterase type 3 inhibitor approved for treatment of intermittent claudication. It decreases platelet aggregation, formation of arterial thrombi, vascular smooth-muscle proliferation, and causes vasodilatation.

The American College of Chest Physicians' (ACCP) 2004 guideline for the symptomatic treatment of chronic limb ischemia recommends a limited role for cilostazol. Cilostazol is recommended for patients with disabling intermittent claudication who do not respond to conservative measures (ie, risk factor modification and exercise) and who are not candidates for surgical- or catheter-based interventions. Cilostazol should not be used with less disabling claudication.

A meta-analysis of 8 randomized, placebo-controlled trials of cilostazol in patients with stable, moderate-to-severe claudication, ranging from 12 to 24 weeks in duration, found that cilostazol significantly increased the maximal walking distance before pain becomes intolerable and increased the walking distance before the onset of claudication pain by 50% and 67%, respectively. A well-designed post-marketing study showed similar results.

The most frequently reported adverse events are headache, diarrhea, abnormal stools, dizziness, and palpitations. Dose-related increases in resting heart rate (5 to 7 beats per minute) have also occurred, along with increased premature ventricular contractions and non-sustained ventricular tachycardia.

Cilostazol is in a pharmacological class that is dangerous to people with severe heart failure. Additional studies designed to determine the risk of heart failure in patients taking cilostazol are needed. As for the current lack of information on the use of cilostazol with clopidogrel, it is important to weigh the necessity of both medications with the risk of bleeding in each individual patient.

Cilostazol was added in the *Formulary* for the maintenance treatment of intermittent claudication. It allows people with intermittent claudication to exercise longer before developing their characteristic leg pain and to walk longer before they have to stop because of pain. Because it takes time for this drug to be fully effective, discontinuation of therapy during a hospitalization could affect the ambulation of patients after their discharge.

CiproDex® Otic is a combination of a fluoroquinolone antibiotic (**ciprofloxacin**) and a corticosteroid (**dexamethasone**) with a labeled indication for otitis media with tympanostomy tubes and otitis externa. Otic fluoroquinolone suspensions are used for various off-labeled otic infections for which there is little scientific evidence of efficacy. However, the otitis media data are considered applicable for other otic infections.

Ofloxacin has been the only otic fluoroquinolone listed in the *Formulary*. Published evidence shows that ciprofloxacin combined with a topical steroid significantly increases clinical cure rates when compared with monotherapy for the treatment of acute otitis media with otorrhea through tympanostomy tubes. Topical steroids are added to a fluoroquinolone to reduce inflammation and enhance clinical response rates.

An additional benefit for CiproDex® Otic Suspension is that it is a sterile product. Another fluoroquinolone-corticosteroid otic agent, **Cipro® HC Otic Suspension** contains **ciprofloxacin** plus **hydrocortisone**, but it is not sterile. This product has been requested through the nonformulary process but will now be unavailable. Ofloxacin otic remains in the *Formulary* as an alternative fluoroquinolone without a corticosteroid.

Codeine liquid has been discontinued by its manufacturer and there is no other identifiable alternative vendor. If it was being used as an antitussive, it is recommended that codeine tablets or guaifenesin plus dextromethorphan liquid be used as an alternative. If a liquid opioid is needed, morphine or oxycodone may be suitable alternatives.

Truvada® is a combination of 2 reverse transcriptase inhibitors, **emtricitabine** (Emtriva®) and **tenofovir** (Viread®), used to treat patients infected with HIV. The rationale for the fixed combination is to reduce the "pill burden" of patients with HIV infections with the goal of improved adherence and therapeutic responses. Instead of taking 2 tablets per day, patients taking Truvada® only take 1 tablet per day. Both of the individual ingredients of Truvada® are listed in the *Formulary*.

Emtricitabine is a synthetic nucleoside analog of cytosine. It was added in the *Formulary* for use in combination with other antiretroviral agents for the treatment of patients infected with HIV. Emtricitabine is structurally similar to lamivudine (3TC), so patients with HIV strains resistant to lamivudine should not be treated with emtricitabine.

Tenofovir is a nucleotide analog of adenosine. It was added in the *Formulary* for use in combination with other drugs for the treatment of HIV infection.

The FDA approved Truvada® because the combination tablet is stable and exhibits the same pharmacokinetic profile as the individual ingredients. Efficacy was based on the data from the individual ingredients.

Cost is not an issue, since the individual ingredients are the same cost as the combination product. However, adding this combination product will add to the hospital's inventory. Therefore, Truvada® was designated nonformulary and not available and will be automatically interchanged to its individual ingredients.

Intravenous pantoprazole and **lansoprazole** were deemed therapeutically equivalent by the P&T Committee. Shands at UF has previously deemed oral proton-pump inhibitors (PPIs) therapeutically equivalent. At this time, pantoprazole remains the oral solid and injectable PPI listed in the *Formulary*. There is no cost advantage to switching to lansoprazole. Many standing orders already list

(continued on next page)

Influenza vaccine: shortcomings or shortages?

The influenza vaccine shortage draws attention to an issue that has been a problem for longer than just this "flu" season…drug shortages. Drug shortages are a problem for most hospitals and clinics around the country. The influenza vaccine crisis drew attention to the shortage problem because it could result in a increased risk of infectious diseases.

In an article published in the *New York Times,* Johnathan Gruber, an economics professor at MIT, states, "In America, market incentives yield innovation, but also uncertainty." In other words, even though the United States foots the bill for much of the world's drug development, we are also the first country to feel the pinch of manufacturing changes and decreased product production. The free market system has its benefits and risks.

The Food and Drug Administration (FDA) has outlined some of the reasons for increased drug shortages over the last 10 years. The following is not every possible cause for shortages, but covers the major reasons.

Production issues, whether attributed to a raw material shortage or problems with manufacturing (eg, costs or work force), quickly result in shortages. However, manufacturing is not the only culprit. Business decisions to discontinue production of drugs, limited manufacturing capacity, and the number of manufacturers producing a specific product also play a role in drug shortages.

Vaccines are particularly vulnerable to market changes. In a news release from the International Vaccine Institute in March 2004, it was noted that the current global capacity for production of monovalent influenza vaccines (a vaccine that contains only 1 viral strain) was no more than 750 million doses per year. The World Health Organization estimated the total global production of trivalent vaccine (ie, the normal 3-strain vaccine) at 260 million doses. This is significant because production would shift from trivalent to monovalent vaccines during a pandemic. However, there are currently no estimates on the global use and demand for influenza vaccine.

Aventis Pasteur, a US distributor of the influenza vaccine, released a news statement in August that the company expected to provide up to 52 million trivalent doses of the influenza vaccine to Americans this flu season. As of 2000, the US population was estimated at 281 million. In an article published by the Centers for Disease Control and Prevention (CDC) that same year, 70 to 76 million people in the United States were considered to be at high risk for influenza. Complicating matters, the World Health Organization estimates each patient could require up to 2 doses of the vaccine during a pandemic.

Not only is the lack of production concerning, but accidents during production can destroy huge batches and greatly affect the amount of product available. This is what happened when the Chiron vaccine was contaminated with bacteria (*Serratia marcescans).*

Due to the use of 50-year-old technology, the methods used to grow the viruses used in vaccines lack advanced safeguards and make the process difficult to control. Influenza vaccine is still grown in fertilized chicken eggs that have been inoculated with the virus. After 3 to 4 days of incubation, the egg whites are decontaminated and prepared for quality control screening. If the FDA finds contamination, the batch is lost. New methods are being studied to attempt addressing the technological inferiority of these methods. Companies are working in laboratories to grow the virus in human, dog, and monkey cells, but the FDA has yet to approve any of these newer methods.

Some countries, including the United States, are beginning to stockpile vaccines in order to cover future shortages. However, stockpiling influenza vaccine in preparation for a pandemic is not an option. Influenza vaccine's composition

(continued on next page)

Formulary update, *from page 2*
pantoprazole, which was considered when keeping pantoprazole IV in the *Formulary*.

Lansoprazole suspension and orally disintegrating tablets (Prevacid® SoluTab®) are alternatives to an injectable PPI for patients who cannot take oral solids. Lansoprazole suspension is at least as effective as intravenous PPIs (when used at comparable doses), and may work better because of the bicarbonate used to make the suspension.

Pantoprazole injection has been plagued by chronic shortages, which has created considerable workload. When product is unavailable, the wholesale switch of patients from parenteral to enteral PPI administration is required. This requires identifying patients, contacting prescribers, changing dosages, etc. Since pantoprazole and lansoprazole are now considered therapeutic equivalents, lansoprazole IV can now be substituted in these instances.

Lansoprazole is more potent than pantoprazole on a milligram-per-milligram basis; however, larger doses of pantoprazole are used, making this difference irrelevant. Pantoprazole 40 mg is equivalent to lansoprazole 30 mg (ie, a 4:3 ratio in potency). This ratio will be used when interchanging from lansoprazole to pantoprazole, and vice versa.

Fosphenytoin is a water-soluble prodrug of phenytoin that has been listed in the *Formulary* for many years. It is used to control generalized seizures and for the prevention and treatment of seizures as a short-term substitute for oral phenytoin.

Because fosphenytoin is water soluble, it does not need to be diluted with propylene glycol and ethanol, like injectable phenytoin. Also, the pH of fosphenytoin is closer to a physiological pH (unlike injectable phenytoin, which is very basic). These formulation changes make infusions of fosphenytoin less likely to cause infusion-site reactions (eg, pain, tissue necrosis with extravasation) and permit intramuscular administration when IV access is not possible.

Unfortunately, fosphenytoin is 9 times more expensive than phenytoin. Fosphenytoin does not have any advantage over diluted intravenous phenytoin in patients with good IV access. Data showing better tolerability of fosphenytoin and phenytoin is based on undiluted phenytoin. Therefore, the criteria for using fosphenytoin have always been limited. A recent audit showed significant cost savings if the original criteria for use had been followed.

Therefore, the P&T Committee approved the restriction of fosphenytoin. Fosphenytoin is now restricted to loading doses in patients without vascular access (ie, intramuscular administration) and maintenance doses in patient meeting the following criteria: pediatric patients weighing less than 30 kg or less than 12 years old; patients with a history of significant cardiovascular disease including (but not limited to) arrhythmias; patients with poor IV access (including patients with difficult to maintain peripheral IV lines or patients receiving fluids or medications through a PICC line or central line that are incompatible with phenytoin; patients with significant peripheral vascular disease; and patients with a history of an adverse reaction to intravenous phenytoin.

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News, *from page 3*
depends on the appearance and identification of the responsible virus at the start of the pandemic.

Since Chiron's announcement that it would not be able to supply the influenza vaccine, the United States Congress has proposed laws to try to address the shortage. The Influenza Vaccine Emergency Act (H.R. 5243) would allow health officials to direct the distribution of the influenza vaccines to high-risk populations. The Influenza Preparation and Vaccination Act (S. 2959) would establish grants to the states to develop influenza vaccine supply and management programs and would guarantee the federal purchase of unused influenza virus vaccine held by grantees. These are some of the possible long-term solutions. In a quick-fix initiative, The Emergency Flu Response Act of 2004 (S. 2968) declared a public health emergency and allowed the importation of vaccine from companies that had not originally been suppliers to the United States. After the declaration, an estimated 5 million imported doses were examined by the FDA. All vaccines imported to the U.S. were received by the government and treated as investigational drugs. Any patients receiving these doses will be required to sign a consent form for administration.

On November 9, 2004, the CDC announced that it would distribute the remaining 10.3 million doses of influenza vaccine from Aventis Pasteur through December and January. This plan takes into account many factors, but the number of high-risk patients is the major determinant in the distribution process.

The recent influenza emergency is not the first, nor will it be the last, shortage. Many resources are available to practitioners and the public. The CDC website (www.cdc.gov) and the ASHP drug shortage website (http://www.ashp.org/shortage) are regularly updated. The CDC has also established a hotline (1-800-CDC-INFO) to provide practitioners and the public with information on the vaccine shortage. As practitioners, we have a duty to our patients to stay informed.

by Brandi Beyhan, PharmD

Avoid these abbreviations... and avoid problems

The following inappropriate abbreviations CANNOT be used to write a valid order. *(See related article on page 1.)*

INAPPROPRIATE ABBREVIATION	APPROPRIATE ABBREVIATION
U	Spell "Units" instead
IU	Spell "International Units" or "Units" instead
µ (Greek mu symbol)	Use "mcg" for micrograms
Doses less than 1 unit	Use leading zero (eg, 0.1 mg)
Doses greater than 1 unit	Do not use trailing zero (eg, 1.0 mg)
QD or OD	Spell "daily" instead
< or >	Spell "less than" or "greater than"
MSO4	Spell "Morphine"
MgSO4	Spell "Magnesium sulfate"
CC	Use "mL" instead