Volume 15, Number 1

SHANDS
at the University of Florida

January 2001

Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met November 21, 2000. 2 drugs were added in the *Formulary* and 1 drug was added for an evaluation. 3 dosage forms were deleted. 3 drugs were designated not available.

◆ ADDED

Gatifloxacin (Tequin® by Bristol-Myers Squibb)

Pantoprazole (Protonix® by Wyeth)

◆ ADDED FOR EVALUATION

Crotalide polyvalent immune fab, ovine (CroFab® by Protherics)

◆ DELETED

Estradiol valerate (eg, Delestrogen® by Bristol-Myers Squibb)

Terbutaline inhaler (Brethaire® by Novartis)

Omeprazole capsules (Prilosec® by Astra)

◆ NONFORMULARY, NOT AVAILABLE

Levofloxacin (Levaquin® by Ortho McNeil)

Omeprazole capsules (Prilosec® by Astra)

Rabeprazole (Aciphex® by Janssen)

Gatifloxacin is a fluoroquinolone antibiotic with activity against gram-positive organisms, particularly respiratory pathogens. When trovafloxacin was removed from the *Formulary*, it created a need to add a fluoroquinolone in the *Formulary* with more gram-positive coverage compared with ciprofloxacin. The

(continued on next page)

THERAPEUTIC INTERCHANGE

Pantoprazole selected as the only proton pump inhibitor

Proton pump inhibitors (PPIs) are among the most commonly prescribed drugs in the United States. They are also commonly used in the hospital setting and Shands at UF is no exception.

For many years, PPIs have been therapeutically interchanged at Shands at UF. Omeprazole has been the PPI listed in the *Formulary*. It was selected over lansoprazole when these 2 PPIs were the only products on the market. There are now 4 different oral PPIs on the market. An injectable PPI may be approved as soon as the 1st quarter of 2001.

The P&T Committee re-evaluated the PPI listed in the *Formulary* and has decided to switch from omeprazole to pantoprazole. Effective January 1, 2001 pantoprazole will be the proton pump inhibitor available at Shands at UF. There will be 1 exception. An extemporaneously prepared omeprazole solution (2 mg/mL) will remain available for use in very young children and in patients with tubes (eg, J-tube). Currently, there is insufficient data to support the use of pantoprazole by this method.

The interchange doses for the "nonformulary-and-not-available" PPIs are listed in the table below. Since pantoprazole is only available as a 40-mg tablet, most of the equivalent dosages are 40 mg once a day.

When these interchanges are made, a new order will be written in the Orders section of the chart. Also, a note will be written in the Progress Notes explaining the interchange.

DRUG / DOSAGE ORDERED	EQUIVALENT PANTOPRAZOLE DOSAGE
Omeprazole (Prilosec®) 10 mg QD	**Pantoprazole (Protonix®)** 40 mg QD
Omeprazole 20 mg QD	Pantoprazole 40 mg QD
Omeprazole 40 mg QD	Pantoprazole 40 mg QD
Omeprazole 20 mg BID	Pantoprazole 40 mg QD
Omeprazole 40 mg BID	Pantoprazole 40 mg BID
Lansoprazole (Prevacid®) 15 mg QD	**Pantoprazole** 40 mg QD
Lansoprazole 15 mg BID	Pantoprazole 40 mg QD
Lansoprazole 30 mg QD	Pantoprazole 40 mg QD
Lansoprazole 30 mg BID	Pantoprazole 40 mg BID
Rabeprazole (Aciphex®) 20 mg QD	**Pantoprazole** 40 mg QD
Rabeprazole 40 mg QD	Pantoprazole 40 mg QD

INSIDE THIS ISSUE

Formulary update, *from page 1*
Anti-Infective Subcommittee of the P&T Committee recommended that gatifloxacin and levofloxacin be deemed therapeutically equivalent and the least expensive product be added in the *Formulary*. The P&T Committee accepted this recommendation; and, subsequently, gatifloxacin was awarded the bid and will be listed in the *Formulary*. **Levofloxacin** has been designated nonformulary and not available.

The P&T approved gatifloxacin criteria-for-use that include community-acquired pneumonia, acute bacterial exacerbation of chronic bronchitis, and acute sinusitis. For community-acquired pneumonia, gatifloxacin is a more cost-effective alternative than the commonly used combination of ceftriaxone plus azithromycin (ie, 1/4th the cost).

Further, like other fluoroquinolones, gatifloxacin has excellent oral bioavailability. For patients who are taking other oral medications or a normal diet, the intravenous route of gatifloxacin will be automatically switched to the oral route. When given orally, gatifloxacin only costs 20% as much as the combination of intravenous ceftriaxone plus azithromycin.

When used for upper respiratory tract infections, the adult dose of gatifloxacin is 400 mg (IV or oral) daily for 7 to 10 days. Because the oral bioavailability of gatifloxacin is nearly 100%, the oral and intravenous doses are the same. Unlike most fluoroquinolones, no significant pharmacokinetic interactions occur when milk or calcium carbonate is administered concomitantly with gatifloxacin. However, other orally administered compounds that contain aluminum salts (eg, antacids), iron salts (eg, multivitamins), magnesium salts, or zinc salts will significantly reduce the oral absorption of gatifloxacin. Didanosine (ddI) may also decrease fluoroquinolone bioavailability due to the buffering agents in the nonenteric-coated tablets, solution, and oral suspension. The above agents should not be taken within 4 hours after gatifloxacin administration.

Pantoprazole is the 4th marketed proton-pump inhibitor (PPI). It has been marketed in other countries for several years. Pantoprazole is similar to omeprazole, which has been listed in the *Formulary*.

Unlike omeprazole, pantoprazole has not been shown to cause significant drug interactions with drugs metabolized by the cytochrome P450 system in the liver (ie, CYP2C19, 3A4, 2D6, and 2C9). Like the other PPIs, pantoprazole does decrease the absorption of drugs that depend on stomach acid for absorption (eg, ketoconazole).

Pantoprazole is available in 40-mg tablets and is usually dosed once a day. No adjustments are needed for patients with impaired renal function. The interchange doses for the other PPIs are listed in *Therapeutic Interchange* article on page 1.

Omeprazole has been deemed nonformulary and not available. **Rabeprazole** is also nonformulary and not available. Lansoprazole already has this designation. Omeprazole extemporaneously compounded liquid will remain available for patients who need this dosage form.

CroFab® is an **ovine polyvalent crotalide immune fab** obtained from the blood of healthy sheep immunized with 1 of the following North American snake venoms: Crotalus *atrox* (Western Diamondback rattlesnake), *Crotalus adamateus* (Eastern Diamondback rattlesnake), *Crotalus scutulatus* (Mojave rattlesnake), and *Agkistrodon piscivorus* (Cottonmouth or Water Moccasin). The fab fractions of immunoglobulins from the 4 different antivenins are combined to make the ovine polyvalent crotalide immune fab.

CroFab® is an orphan drug with a labeled indication for the management of patients with minimal or moderate North American rattlesnake envenomations. Early use (ie, within 6 hours) is advised to prevent clinical deterioration and the occurrence of systemic coagulation abnormalities.

CroFab® was added in the *Formulary* because of the shortage of Antivenin Polyvalent. The production of Antivenin Polyvalent has been suspended since last February because of quality control problems at the manufacturing facility. Although Antivenin Polyvalent has been available on an emergency basis, a letter from the manufacturer stated that there might be instances where the product is unavailable. CroFab® offers an alternative and has been added in the *Formulary* for a year to cover the next rattlesnake season.

CroFab® is being promoted as having a better safety profile than Antivenin Polyvalent. The risk of serum sickness may be less. Both products are very expensive with a typical treatment dose costing $6000 to $9000.

Estradiol valerate injection is a long-acting dosage form of estradiol. Estradiol valerate is a depot injection in oil, which slows absorption after intramuscular injection. Esterification of estradiol to estradiol valerate significantly increases the parenteral duration of action compared to aqueous estradiol formulations.

The manufacturer of estradiol valerate has stopped making this dosage form; therefore, it has been deleted from the *Formulary*. In August, estradiol valerate was recalled because of quality control problems at the manufacturing plant. Although various manufacturers listed this product, 1 company made all products. When the sole manufacture decided to stop making estradiol valerate, it became unavailable.

Terbutaline inhalers were removed from the *Formulary* because equally effective alternatives for acute bronchospasm, like albuterol inhalers, can be used instead. Terbutaline inhalers are rarely used in the ambulatory setting and there is very little demand for this product. Like albuterol, terbutaline is an beta2-adrenergic receptor agonist.

SHORTAGES

Tetanus toxoid in short supply, but…

There is a nationwide shortage of tetanus toxoid; however, at this time Shands at UF is able to get a limited supply of both tetanus toxoid and tetanus and diphtheria toxoids (Td). An allocated amount of the multidose vials of both tetanus toxoid and Td are available each week; thus the shortage has not yet cause *major* concerns here. The unit-dose syringes are not available, however. Thus, the Shands IV Center must draw up doses into syringes. The Emergency Department (ED) is using the multi-dose vials and drawing up each dose as needed.

This shortage resulted from 2 coincident situations: 1) a decrease in the number of lots of Td released by Wyeth Lederle, and 2) a temporary decrease in inventory of Td following routine maintenance activities at the production facilities by Aventis Pasteur that lasted longer than anticipated. Approximately half of the usual number of Td doses has been distributed this year. Although there have been no decreases in production of tetanus toxoid, availability is low because of increased use during the Td shortage. On the basis of information provided by Aventis Pasteur, vaccine supplies should be restored early in 2001. Until then, Aventis Pasteur will be limiting orders to assure the widest possible distribution of available doses.

(continued on next page)

ANTI-INFECTIVE UPDATE

Tamiflu®: Test not required

Oseltamivir was added in the *Formulary* in September 2000. This antiviral has activity against both influenza A and B and was added for use in debilitated patients (eg, immunocompromised patients).

Because there were concerns about inappropriate over-prescribing, a restriction was put on the use of oseltamivir. Oseltamivir could only be used if a rapid test for influenza A and B was ordered. The 2nd day's doses would only be dispensed if the test was positive. However, this restriction was lifted because the test is not considered to be reliable.

Published studies show that the rapid influenza test is greater than 90% accurate. Studies done here at Shands at UF based on samples taken from patients with positive viral cultures for influenza A or B were not as reliable. Instead of >90% accuracy, only 50% or less of these culture-positive patients were positive using the rapid test. This questions whether the influenza quick test should be used at all. Thus, the diagnosis of influenza should be based on clinical symptoms.

All of the following 3 diagnostic criteria must be met or the patient has to have a positive antigen test or culture for influenza A or B virus. The patient 1) must have respiratory tract symptoms [ie, cough], 2) must have a fever or other systemic symptoms [malaise, myalgias, chills], and 3) must have these symptoms in the influenza season [winter months or when influenza is known to be circulating in the community]. At the end of this influenza season, an audit of the use of oseltamivir will be done to determine the appropriateness of its use and whether additional restrictions are needed.

Zosyn®: ID Consult required

In April 2000, the P&T Committee designated Zosyn® nonformulary and not available through the normal nonformulary process. Because there may be a rare patient with an organism sensitive to Zosyn® and resistant to the agents listed in the *Formulary*, Zosyn® use was allowed after a clinical pharmacist reviewed the culture and sensitivity report. This process did not avoid the use of Zosyn® in patients who had culture positive results, but who were not infected (eg, colonization). In order to allow the appropriate diagnosis before the use of Zosyn®, an ID Consult is now needed before Zosyn® can be used nonformulary.

Linezolid: Criteria for use

Linezolid was added in the *Formulary* in October 2000. Prior to admission in the *Formulary*, it was available nonformulary only after an ID Consult. When listed in the *Formulary*, this restriction was continued.

Linezolid is a novel antibacterial agent that has clinical utility in the treatment of infections caused by resistant aerobic gram-positive bacteria. It can be used in patients infected with vancomycin-resistant enterococcus or methicillin-resistant staphylococcus. Because of its utility in resistant infections, linezolid needs to be reserved for these difficult infections. Overuse could decrease the utility of this valuable agent.

The P&T Committee has approved the use of linezolid in 2 situations: the treatment of serious infections caused by vancomycin-resistant *Enterococcus faecium* and *Enterococcus faecalis* or the treatment of serious gram-positive infections in patients who fail or who are intolerant of other therapies (ie, vancomycin). Agents that are less toxic and less expensive should be used for other indications.

Synercid®: Criteria for use

Synercid® (quinupristin plus dalfopristin) was added in the *Formulary* in November 1999. Like linezolid, Synercid® requires an ID Consult before it will be dispensed. Also like linezolid, it should be reserved for resistant organisms.

The P&T Committee has approved 2 uses for Synercid®. Synercid® should be used for the treatment of serious infections caused by vancomycin resistant *Enterococcus faecium*. It is not active against *Enterococcus faecalis*. Synercid® may also be useful in the treatment of serious gram-positive infections in patients who fail or who are intolerant to other therapies (ie, vancomycin or linezolid). Due to the cost, ease of administration (does not require a central line) and oral availability, linezolid is considered the preferred agent over Synercid® for susceptible organisms. Synercid® is considered a 3rd-line agent after linezolid.

Shortages, *from page 2*

The shortage impacts persons aged ≥ 7 years who require tetanus prophylaxis in wound management, have not completed a primary series (3 doses) of vaccine containing Td, or have not been vaccinated during the preceding 10 years with Td, diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) or diphtheria and tetanus toxoids (DT). This shortage will not affect vaccination of children aged < 7 years who require additional doses of a vaccine containing tetanus toxoid; they should receive DTaP or pediatric DT, which are not in short supply.

Td is preferred to tetanus toxoid because Td provides protection against both tetanus and diphtheria. However, during this shortage, if Td is not available, tetanus toxoid can be used as an alternative for persons aged ≥ 7 years who require immediate boosting with tetanus (eg, wound management), or who are unlikely to return to a clinic if vaccination is delayed. If tetanus toxoid is administered, patients and healthcare providers must weigh the risks and benefits of subsequent vaccination with Td. Arthus-type reactions may occur among persons who receive multiple doses of tetanus toxoid, especially within short intervals (< 10 years). However, if vaccination with Td is delayed for > 10 years following their last Td administration, persons may be protected inadequately against diphtheria. After the shortage is resolved, Td should again be considered preferable to tetanus toxoid.

The CDC recommends that clinics experiencing shortages of Td prioritize their use of available supplies. If administration of Td is delayed, clinics should implement a callback system when vaccine is available. Recommendations for use (highest to lowest priority) of Td are:

1. Persons traveling to a country where the risk for diphtheria is high.*
2. Persons requiring tetanus vaccination for prophylaxis in wound management.
3. Persons who have received < 3 doses of vaccine containing Td.
4. Pregnant women and persons at occupational risk for tetanus-prone injuries who have not been vaccinated with Td within the preceding 10 years.
5. Adolescents who have not been vaccinated with a vaccine containing Td within the preceding 10 years.
6. Adults who have not been vaccinated with Td within the preceding 10 years.

*Travelers to certain countries may be at substantial risk for exposure to toxigenic strains of *C. diphtheriae*, especially with prolonged travel, extensive contact with children, or exposure to poor hygiene. On the basis of surveillance data and consultation with the World Health Organization, countries with highest risk are in Africa (Algeria, Egypt, and sub-Saharan Africa); the Americas (Brazil, Dominican Republic, Ecuador, and Haiti); Asia/Oceania (Afghanistan, Bangladesh, Cambodia, China, India, Indonesia, Iran, Iraq, Laos, Mongolia, Myanmar, Nepal, Pakistan, Philippines, Syria, Thailand, Turkey, Vietnam, and Yemen); and Europe (Albania and all countries of the former Soviet Union).

Drugs & Therapy
B • U • L • L • E • T • I • N

Volume 15, No. 1 January 2001

This publication is produced by the Drug Information and Pharmacy Resource Center under the direction of the Department of Pharmacy Services and the Pharmacy and Therapeutics Committee.

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PO Box 100316
Gainesville, FL 32610-0316

NON-PROFIT ORG.
U.S. POSTAGE
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GAINESVILLE, FL
PERMIT NO. 286

OUTPATIENT PHARMACY

4 brand name drugs — update

In the June 2000 issue of the *Bulletin,* we reported that the legislature changed the healthcare benefits for patients with Medicaid that limits the number of brand name drugs that will be covered as part of the Medicaid drug benefit. Patients are now limited to 4 brand name drugs per month. The original legislation excluded anti-retrovirals, mental health drugs, contraceptives, and diabetic supplies from the limit. Recently, immunosuppressive drugs were also excluded, which is welcome relief for our transplant patients.

The 4-brand-name-drug limit has had a big impact on Medicaid patients. As predicted, many patients had to scramble to find less expensive alternatives for their brand name prescriptions when the change was implemented in September. Because of their limited funds, many patients have to change their drug therapy or choose not to have some of their prescriptions refilled. Patients have starting paying cash for their less expensive medications. They are using more generics. Many patients on proton pump inhibitors, which are only available as brand name products, have been switched to a H2-blocker. Generic enalapril has become a popular ACE-inhibitor. Cerivastatin is commonly being used as an HMG-CoA inhibitor. Although cerivastatin is a brand-name drug, it only costs 10 to 20% of other HMG-CoA inhibitors at Shands Pharmacies. This can have a large impact on low-income patients who are paying "out of their pocket."

The 4-brand-name-drug limit has had a big impact on Medicaid patients. As predicted, many patients had to scramble to find less expensive alternatives for their brand name prescriptions when the change was implemented in September.

There is a phone number that a prescriber can call to try to get an exception to the 4-brand-name limit for medical reasons. The prescriber can call (877) 553-7481. A pharmacy cannot get an exception approved. The prescriber must make the call.

This program, once again, emphasizes the importance of prescribers knowing how their patients pay for their prescriptions. It is recommended that patients be asked, "How do you pay for your medications?" before the prescription is written. Medicaid and other 3rd-party payers have limits on what is covered. By asking this question, modifications in the prescription can be made *before* the patient is at the pharmacy and cannot pay for their medication. It will also help you avoid telephone calls and pages to get a patient's prescriptions changed.

A medication regimen review may be able to identify drugs that could be switched to generic alternatives or which brand name drugs would cost the patient the least out-or-pocket expenses. The clinical staff in the Outpatient Pharmacy may be able to help. You can get assistance by contacting the Shands Medical Plaza Pharmacy by calling 265-8276, or by e-mailing Bill Harbilas, PharmD, at harbijw@shands.ufl.edu