

Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met April 19, 2011. 7 products were added in the *Formulary*; 7 were deleted, while 13 products were designated nonformulary and not available. 3 interchanges were modified. 4 criteria for use were approved including 2 restriction changes.

◆ ADDED

Abacavir-Lamivudine
(Epzicom[®] by GlaxoSmithKline)

Dakin's Solution
(by Century Pharmaceuticals)

Glatiramer Acetate
(Copaxone[®] by Teva)

**Pantoprazole Tablets/
Suspension** (Generic)

Pilocarpine Tablet (Generic)

Testosterone Gel
(AndroGel[®] by Abbott)

◆ DELETED

Esomeprazole Injection
(Nexium[®] by AstraZeneca)*

*Nonformulary and not available

**Lansoprazole Capsules/
Suspension** (Generic)*

Mexiletine 200-mg Capsules
(Generic)*

Omeprazole Tablets/Suspension
(Generic)*

Oxychlorosene (Clorpactin[®])*

◆ NONFORMULARY AND NOT AVAILABLE

Adenovirus Vaccine
(no brand name)

Testosterone Buccal

Testosterone Gels (Multiple)†

†Except AndroGel[®]

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NEWS

Prescription drug trends 2010

The IMS Institute for Healthcare Informatics recently released its report *The Use of Medicines in the United States: Review of 2010*. This report provides insights into prescription drug use last year. For example, \$307 billion was spent on prescription drugs, a 2.3% increase over the previous year. Costs increased 3% in the institutional setting but only 2% in the community setting. Costs for branded "small molecules," although still the largest segment of the market, grew more slowly than biologics, which increased at a faster pace.

Oral medications increased only slightly (0.5% or -0.3% adjusted on a per-capita basis). Injectables also increased only slightly (0.2% or -0.6% adjusted). The number of retail prescriptions dispensed was still nearly 4 billion. This was a historically low increase of 1.2% and was correlated with a decrease of 4.2% of physician office visits. The number of patients being started on medications for a chronic condition decreased and, more often, they were started on a generic drug.

Commercial insurance covered 63% of prescriptions dispensed, while 22% were Medicare Part D prescriptions. Medicaid increased to 8.4% of all prescriptions. Only 6.9% of all prescriptions were paid for by the patient without some type of third-party coverage (eg, commercial, Medicare, or Medicaid). The average prescription co-pay was \$10.73, which represented a 1.8% decline. This decline is attributed to the increased use of generics. Brand-name drug co-pays increased over 7% for both preferred and non-preferred brands. The average co-payment for these brand-name drugs was \$23.65 and \$34.77, respectively.

Generics now make up 78% of all prescriptions dispensed. When a brand product becomes available as a generic, 80% of the use of that drug is a generic within 6 months. This continues to mitigate increased total spending on prescription drugs despite large increases in brand-name prices.

Drug therapy for 17 chronic conditions made up 38% of all prescriptions and

nearly half (47%) of all drug expenditures. These diseases or conditions include attention deficit hyperactivity disorder (ADHD), Alzheimer's disease, benign prostatic hypertrophy (BPH), hypercholesterolemia, asthma-chronic obstructive pulmonary disease (COPD), depression, diabetes, HIV, hypertension, insomnia, migraines, overactive bladder, osteoporosis, Parkinson's disease, gastric acid conditions (PPIs), antipsychotics, and seizure medications. The 5 classes with the highest spending include cancer drugs, respiratory drugs, lipid regulators, antidiabetic agents, and antipsychotics. These 5 classes account for \$93.3 billion of all drug expenditures, which is nearly a third of all expenditures. Although cancer drugs lead expenditures, the rate of spending growth continues to slow.

Lipitor[®] (atorvastatin) continued to lead expenditures for a specific drug, accounting for \$8.6 billion. A generic version of Lipitor[®] will be available before the end of this year. Nexium[®] (esomeprazole) is second, with \$5.1 billion in sales. This is particularly surprising since many other proton-pump inhibitors are available as generics (eg, lansoprazole, omeprazole, and pantoprazole). Plavix[®] (clopidogrel) is third, with \$2.9 billion in sales. Plavix[®] should be available as a generic in May 2012, 1 year from now. Advair[®] (fluticasone-salmeterol) is fourth, with \$3.9 billion in sales. Although the patent for Advair[®] expires this year, a generic has been slow to be developed because of the delivery method for the dry-powder inhaler (ie, Diskus device). Abilify[®] (aripiprazole) is fifth, with \$1.9 billion in sales.

Once again, hydrocodone-acetaminophen combinations are the highest volume prescription drug with 3.7 billion prescriptions! Simvastatin, lisinopril, levothyroxine, amlodipine, omeprazole (prescription only), azithromycin, amoxicillin, metformin, and hydrochlorothiazide round out the top 10 drugs in term of the volume of prescriptions. Overuse of antibiotics like azithromycin and amoxicillin contribute to resistant strains of bacteria.

◆ **NONFORMULARY AND NOT AVAILABLE (cont.)**

Testosterone Implants

Testosterone Patch (Androderm®)

Testosterone Topical Solution/
Sprays

◆ **INTERCHANGES**

Cefoxitin for Cefotetan†

†During the cefotetan shortage

Dakin's Solution for
Oxychlorosene

Pantoprazole (oral, suspension,
& IV) for all other PPIs

◆ **CRITERIA-FOR-USE CHANGES**

Influenza Vaccine

Nicotine Gum/Patch

Promethazine IV

Epzicom® is a combination anti-retroviral product used in combination with other antiretroviral agents for managing treatment-naïve and experienced patients infected with HIV. Currently, Shands at UF has both **lamivudine** and **abacavir** as individual items listed in the *Formulary*. Therefore, the combination product was added in response to nonformulary use. This minimizes the risk of non-adherence, which may occur when administering individual products upon admission or discharge.

Dakin's Solution was developed in the early 1900s as a wound-irrigating solution with antiseptic properties. It contained highly diluted sodium hypochlorite (ie, bleach). Full-strength Dakin's Solution is sodium hypochlorite 0.5%. Half-strength is 0.25% sodium hypochlorite and quarter-strength Dakin's Solution is 0.125% sodium hypochlorite. This can be confusing. A recent issue of the *ISMP Medication Safety Alert* highlights this issue (ie, full-strength is 0.5% while half-strength is 0.25%). This article also warns that Dakin's Solution can be as harmful to fibroblasts as bacteria.

In 1989, the P&T Committee deleted Dakin's Solution from the *Formulary* and approved a therapeutic interchange to sodium oxychlorosene (Clorpactin®). Sodium oxychlorosene is a complex chlorine-releasing antiseptic similar to Dakin's Solution that is used topically as an irrigating solution. At the time, sodium oxychlorosene was much more convenient to use because it came as a powder that could be diluted just prior to use. Dakin's solution was stable for only 72 hours after mixing. Dakin's Solu-

tion now comes as a pre-mixed solution, which is more convenient. Nurses no longer have to mix oxychlorosene at the bedside. Dakin's Solution was added in the *Formulary* with the automatic interchange from oxychlorosene to Dakin's using the same conversion as previously approved.

DAKIN'S SOLUTION INTERCHANGE

PRODUCT DISPENSED..... PRODUCT ORDERED

Full Strength (0.5%) Dakin's for Clorpactin 4 grams/Liter of water

Half Strength (0.25%) Dakin's for Clorpactin 2 grams/Liter of water

Quarter Strength (0.125%) Dakin's for Clorpactin 1 gram/Liter of water

Glatiramer acetate was evaluated for possible addition in the *Formulary* because it is used nonformulary in 3 or more patients during some months.

Treatments for multiple sclerosis (MS) are selected according to the type of multiple sclerosis. Glatiramer acetate is a biologic response modifier that has a labeled indication for the treatment of relapsing-remitting multiple sclerosis (RRMS) and for prolonging the time to clinically definite multiple sclerosis in patients with a first clinical episode consistent with MS.

Glatiramer's pharmacology is not completely understood; however, it is thought to be neuroprotective in RRMS by acting as a decoy to prevent an autoimmune attack on myelin. Thus, the axonal loss and demyelination, as well as an inflammatory component, will be reduced via glatiramer therapy. It is unclear how this translates into long-term outcomes.

Copaxone® is injected subcutaneously daily, rotating injection sites so as not to inject into the same spot more than once weekly. It is partially hydrolyzed at the injection site. Some is thought to enter into the lymphatic and systemic circulation.

Efficacy data show a benefit over placebo in RRMS, particularly in reducing the number of relapses and hospitalizations. When compared to other agents for the same indication, studies show no significant difference among the treatments, though there are limitations of the studies. Copaxone® has also been shown to be as effective in prolonging the time to clinically definite MS, although reports are conflicting.

Glatiramer is expensive. Interferon beta-1a injection, which is given 3 times weekly, is expensive, but less expensive than glatiramer.

Glatiramer was added in the *Formulary* for treatment of a patient who is intolerant to, or unresponsive to treatment with, interferon beta-1a or 1b, as these alternatives show similar efficacy, lower acquisition cost, and more convenient dosing. Additionally, it is available for cases of treatment

continuation for a patient already on glatiramer at the time of admission.

Pantoprazole is a proton-pump inhibitor (PPI) used orally as a tablet or extemporaneously compounded suspension and intravenously to decrease the production of stomach acid. PPIs have been deemed thera-

apeutically equivalent by the P&T Committee for many years. The preferred agent has changed multiple times in order to select the product that is the least costly.

In February 2010, the P&T Committee revised the PPIs listed in the *Formulary* to include products that would avoid the potential interaction between esomeprazole or omeprazole and clopidogrel. This complicated the formulary listings but was necessary to avoid a large increase in expenditures.

Now that there are multiple generic sources for oral pantoprazole, it is favorable economically (approximately a \$50,000 savings) and logistically (ie, same tablet, suspension, and IV PPI) to add the **oral** and **suspension** dosage forms of pantoprazole in the *Formulary*, and delete **esomeprazole IV** and **omeprazole** and **lansoprazole oral (tablets and suspension)** and designate them nonformulary and not available. All PPIs will be interchanged to pantoprazole, which does not have the same concern as omeprazole and esomeprazole when used with clopidogrel. Pantoprazole should not prevent the conversion of clopidogrel to its active form...if that is truly a significant interaction with esomeprazole and omeprazole. The IV to PO [oral] policy allows pharmacists to switch from IV to oral pantoprazole when patients are taking other medications orally [and it is not used as a constant infusion for a GI bleed]. The table at the top of the next page summarizes this interchange.

Pilocarpine tablets are approved for use in Sjögren Syndrome and for xerostomia associated with radiation. Non-FDA labeled uses are for drug-induced dry mouth or for prophylaxis when chemotherapy-induced mucositis is anticipated. Different modalities for dealing with deficient salivation include sipping water regularly, using artificial saliva, chewing gum (preferably sugar-free), avoiding or substituting anticholinergics, and adding on

(continued on next page)

PROTON-PUMP INHIBITOR (PPI) INTERCHANGE*†‡

ORDERED DRUG	INTERCHANGED TO:
Oral Orders (ie, capsules, tablets, and suspensions)†	
Lansoprazole 15 mg	Pantoprazole 20 mg (same interval)
Omeprazole 10 mg	
Rabeprazole 10 mg	
Dexlansoprazole 30 mg	Pantoprazole 40 mg (same interval)
Esomeprazole 20 mg	
Lansoprazole 30 mg	
Omeprazole 20 mg	
Rabeprazole 20 mg	
Dexlansoprazole 60 mg	Pantoprazole 80 mg (same interval)
Esomeprazole 40 mg	
Lansoprazole 60 mg	
Omeprazole 40 mg	
Rabeprazole 40 mg	
IV Orders	
Esomeprazole 20 mg IVPB	Pantoprazole 40 mg IVPB
Esomeprazole 40 mg IVPB	Pantoprazole 80 mg IVPB
Esomeprazole 80 mg IVPB	Pantoprazole 80 mg IVPB
Esomeprazole 8 mg IV/hr	Pantoprazole 8 mg IV/hr

*All oral PPIs will be interchanged to pantoprazole; however, patients may use their own supply of medication from home if specified in the order. Dexlansoprazole [Dexilant®], Esomeprazole [Nexium®], Lansoprazole, Omeprazole, and Rabeprazole [AcipHex®] are non-formulary and not available (ie, will not be supplied by Shands).

†Pantoprazole suspension (equal dose) can be substituted for tablets when the patient cannot take a tablet

‡Pantoprazole oral (tablet or suspension) can be substituted for the IV route when patients are taking other medication AND it is not high-dose constant infusion for a GI bleed.

§Pediatric patients will be interchanged on a mg/kg-basis, if necessary.

pharmacological agents that stimulate salivation. The relative safety, efficacy, and low cost of pilocarpine supports its use as a first-line therapy in xerostomia associated with Sjögren Syndrome and radiation therapy. Adverse effects are rare, with most adverse effects being well tolerated.

Testosterone prescriptions have increased dramatically over the past 10 years to treat hypogonadism in men. The most common complications of testosterone deficiency include decreased libido, fatigue, sweating, muscular atrophy, and osteoporosis. Up to 25% of men over 50 years of age will have testosterone levels under the normal threshold and will be diagnosed with hypogonadism.

Testosterone products are Schedule III controlled substances. Therefore, patients are not permitted to use their outpatient prescriptions when they are admitted in the hospital.

Currently, there are many testosterone products that are either available or soon to enter the market. These include injections, implants, capsules, buccal tablets, topical creams, ointments, gels, solutions, and patches. These products have different pharmacokinetic properties and data are lacking on how best to switch between formulations. One clinical trial compared injectable and gel testosterone preparations. The outcomes included serum testosterone levels and quality of life. The study resulted in greater fluctuations in testosterone levels in the injectable versus topical group; this is consistent with the pharmacokinetic properties of the different formulations.

Since there are a variety of products available and it is not feasible to supply them all, a **testosterone gel** was listed in the *Formulary*. Although a brief interruption of therapy will likely not result in serious outcomes, patients may

experience symptomatic effects from missed doses. Long-term sequelae would take months to years to occur.

To convert a patient from another topical preparation to Androgel®, simply use the standard prescribing information. The typical starting dose is 5 mg (1 packet); however, a patient who is on a large dose of a topical testosterone could be converted to 10 mg (2 packets). The dose is usually given in the morning to clean, dry, intact skin of the shoulder and upper arms and/or abdomen. The entire contents of the packet is squeezed on the site of administration then spread with a gloved hand to avoid systemic exposure. The area administered should be covered with clothing after the gel dries to prevent secondary transfer of drug.

Injectable testosterone is an option for patients admitted for an extended period. However, testosterone levels need to be monitored.

Testim® (testosterone gel), **Fortesta®** (testosterone gel), **Axiron®** (testosterone topical solution), **Androderm®** (testosterone topical patch), **Testopel®** (testosterone subcutaneous implant), and **Striant®** (testosterone buccal tablets) were designated nonformulary and not available [and patients cannot use their supply from home].

Mexiletine is an oral antiarrhythmic agent with a labeled indication for the treatment of life-threatening ventricular arrhythmias. It is used off label for neuropathic pain and diabetic neuropathy. The sole manufacturer of mexiletine 200-mg capsules (Teva) has discontinued this dosage strength. Therefore, this strength was deleted from the *Formulary*. The 150-mg and 250-mg capsules are still available.

Adenovirus vaccine is a live oral vaccine with a labeled indication for the prevention of febrile acute respiratory disease caused by adenoviruses (serotypes 4 and 7). It is approved for use in military populations 17 through 50 years of age. A clinical trial performed in military recruits (greater than 4000 patients) showed a significant reduction in recruits with respiratory disease when given the vaccine (1 vs 48 recruits for vaccine and placebo, respectively). Overall, it was well tolerated in this population with adverse events rates similar to placebo.

Vaccinees and individuals who come in contact with vaccinees may be exposed to the vaccine viruses shed in the stool for up to 28 days. Vaccinees should exercise caution when in close contact with children less than 7 years of age, immunocompromised individuals, and pregnant women during the 28 days following vaccination. (continued on next page)

Formulary update, from page 3

Cefotetan is a second-generation cephalosporin similar to **cefoxitin**. The P&T Committee has long designated these antibiotics interchangeable. However, cefoxitin, which is also a second-generation cephalosporin, has activity against mycobacteria. This is the only reason it has been listed in the *Formulary* with cefotetan.

There is a nationwide shortage of cefotetan that originally was attributed to a problem with the raw materials. Like most shortages, it is unclear when it will be resolved; however, late second quarter of 2011 has been predicted.

During the shortage, orders for cefotetan will be interchanged to cefoxitin using the guidelines shown on the charts on page 6.

Influenza vaccine changes each year to prevent “the flu” based on the strains predicted to cause infections during the influenza season. Typically, influenza vaccination (barring any shortages) occurs from October to March of each year. Vaccination is initiated in early Fall in order to ensure proper antibody protection prior to the peak of influenza season (January to March for most areas). With concerns for ongoing influenza-related hospitalizations and a reasonable safety profile for the influenza vaccine, an extension of the vaccination period was approved by the P&T Committee.

Influenza hospitalizations are decreasing locally and nationally; low-levels of virus are circulating in the area. Typically, this would be considered a point where we could consider discontinuing the vaccination program as the risk for adverse events increases without enhanced protection against incoming strains from the Southern Hemisphere.

But, in contrast to prior years, the vaccine being developed for 2011–2012 season contains the same 3 strains of influenza from the current vaccine. Therefore, if the same strains are believed to be circulating for the 2011–2012 influenza season, then continuing the vaccination program (while supplies last) is rational and was supported by the Anti-Infective Subcommittee. The vaccination period was extended until our influenza vaccine supplies are exhausted.

Nicotine gum was added in the *Formulary* in October 2009 when the Health Science Center went tobacco-free. Nicotine gum was intended to be an alternative to **nicotine patches**, which were already listed in the *Formulary*, for the treatment of nicotine withdrawal, since patients cannot smoke.

The *Nicotine Treatment Order Form* was based on benchmarking information from other hospitals. The form provides treatment options, doses, and monitoring parameters for both nicotine withdrawal symptoms and possible adverse effects for the treatment options.

The use of these products, especially the patch, is so common that the use of the *Nicotine Treatment Order Form* has been unpopular and difficult to enforce. Therefore, the restrictions on both nicotine gum and patches were lifted. The form remains available for those who want to use it, but it is no longer required.

The continued use of **intravenous promethazine** at Shands at UF has been an ongoing safety concern. Currently, we use labeling as a safety mechanism, which is a low-level method of safety promotion. Some institutions have eliminated intravenous promethazine from their formularies, which is the highest level of error prevention. Currently, we use a large amount of intravenous promethazine, so getting input on a

(continued on next page)

Formulary update, from page 4

proposed deletion was difficult. Therefore, a proposal to delete promethazine from the *Formulary* was published in the *Drugs & Therapy Bulletin* in March.

Many comments were received; most disagreed with the proposal. The Department of Anesthesiology submitted most of the negative comments, but comments were received from the Departments of Medicine, Surgery, Pediatrics, and Emergency Medicine.

Most commentators stated they did not support the proposal without providing a specific rationale for their lack of support [other than promethazine is effective]. Several commentators justified their opposition by stating that IV promethazine was no more dangerous than other IV medications. Specific reasons for opposition to the proposal included that promethazine is listed in antiemetic guidelines, patient preference or satisfaction, and use of IV promethazine may avoid other costs.

The P&T Committee concluded that there is insufficient support to proceed with the proposal to delete promethazine from the *Formulary*. However, additional safety mechanisms were implemented. Promethazine was removed from adult or pediatric EPIC order sets. Nurses must now administer IV promethazine using a dilution and flush syringe and placing the syringe on the Alaris pump with a clip adapter. Standardized administration instructions will be included in EPIC. Direct physician administration (eg, OR) is still permitted. There will be a 1-year evaluation of serious adverse drug reactions to prochlorperazine.

Oral, rectal, and IM promethazine remain options that will be promoted. These options can be added to order sets after EPIC is implemented. Prochlorperazine can be used as an alternative IV agent, but possible adverse effects (ie, unintended consequences of using prochlorperazine over promethazine) will be monitored.

Drug information questions?

Contact the Drug Information Service



Call 265-0408



Or submit your question online at www.shands.org/professionals/druginfo/default.asp

- This service is for referring physicians and other healthcare professionals taking care of Shands patients
- Phones are staffed from 9 am to 4:30 pm, Monday – Friday
- All answers are thoroughly researched and referenced

For emergent questions that do not need thorough research, go to the pharmacy servicing your area.

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CEFOTETAN-TO-CEFOXITIN INTERCHANGE PROCESS

INFECTION SEVERITY	CEFOTETAN	CEFOXITIN
Moderate-to-severe Infections	1 – 2 g IV q8h – q12h	1 – 2 g IV q6h
Life-threatening Infections	3 g IV q8h – q12h	2 g IV q4h
Surgical Prophylaxis		
Pre-operative	1 or 2 g	1 or 2 g
Post-operative	1 or 2 g q8h – q12h	1 or 2 g IV q6h x 2 doses

DOSAGE ADJUSTMENTS FOR MODERATE-TO-SEVERE INFECTIONS

CRCL (ML/MIN)	CEFOXITIN DOSING
> 50	1 – 2 g IV q6h
30 – 50	1 – 2 g IV q8h
10 – 29	1 – 2 g IV q12h
< 10	1 – 2 g IV q24h

DOSAGE ADJUSTMENT FOR LIFE-THREATENING INFECTIONS

CRCL (ML/MIN)	CEFOXITIN DOSING
> 50	2 g IV q4h
30 – 50	2 g IV q6h
10 – 29	2 g IV q8h
< 10	2 g IV q12h