

Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met October 18, 2005. 4 products were added in the *Formulary* and 2 were deleted. 1 dosage form was evaluated and designated nonformulary and not available, and 2 drugs were evaluated, but not added. Criteria for use were modified for 3 drugs.

◆ ADDED

Clozapine Tablets
(generic by IVAX)

Glutaraldehyde 0.6% Solution
(compounded)

Levofloxacin
(Levaquin® by Ortho McNeil)*

Ondansetron Tablets
(Zofran® by GlaxoSmithKline)

*Restricted to ID approval

◆ DELETED

Estradiol Valerate (generic)

Magic Mouthwash
(compounded)**

**Nonformulary and not available,
effective December 1, 2005

◆ NONFORMULARY AND NOT AVAILABLE

Clozapine Orally-Disintegrating Tablets
(FazaClo® by Alamo Pharmaceuticals)

◆ EVALUATED, BUT NOT ADDED

Duloxetine
(Cymbalta® by Eli Lilly)

Mycophenolate Extended-Release (Myfortic® by Novartis)

◆ CRITERIA FOR USE CHANGED

Cefepime (Maxipime® by Elan)***

Ciprofloxacin
(Cipro® and generics)***

Gatifloxacin (Tequin® by Bristol Myers Squibb)***

***Streamlining by the Anti-Infective Stewardship Program approved

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MEDICATION SAFETY

Slang terms and jargon can cause medication errors

This month “Magic Mouthwash” was deleted from the *Formulary* (see *Formulary Update*). The P&T Committee took this action for medication safety reasons. This continues the policy of not allowing the use of non-specific terms for mixtures that have traditionally been used.

Terms like “Magic Mouthwash” are slang, jargon, or coined phrases for mixtures that have a specific purpose. In this instance, the “magic” is pain reduction in patients who have mucositis of the mouth. Mucositis is a very painful condition in patients receiving aggressive cytotoxic chemotherapy.

The logic behind Magic Mouthwash was to combine ingredients with different potential mechanisms of action. The Magic Mouthwash mixture that has been used at Shands at UF contained lidocaine viscous as a local anesthetic, diphenhydramine (Benadryl®) elixir as another local anesthetic, and nystatin suspension as an antifungal. The most commonly used Magic Mouthwash contains equal parts of lidocaine viscous, diphenhydramine elixir, and aluminum-magnesium hydroxide (Maalox®). The antacid was included as a protectant. This “lidobenalox” or BMX (Benadryl-Maalox-Xylocaine) mouthrinse is “swished and swallowed” or “swished and spit.”

Unfortunately, there is no standard for Magic Mouthwash. Some versions contain nystatin to treat fungal infections or hydrocortisone or dexamethasone as anti-inflammatories. Some versions contain sucralfate instead of aluminum-magnesium hydroxide. There are even listed formulas that contain antibiotics like tetracycline or sulfamethoxazole-trimethoprim (Septra®).

Problems can arise when patients receive a product different than what the prescriber intended. The patient could have an allergy to one of the ingredi-

ents. An allergy screen would not be done, unless the individual ingredients are appreciated.

Magic Mouthwash will no longer be dispensed at Shands UF because there is no evidence that it works better than a plain saline rinse.

This action follows the banning of the term “Butt Paste” several years ago. Like Magic Mouthwash, Butt Paste is a nonspecific mixture of ingredients. The “Butt Paste” mixture contained Questran Light® (cholestyramine) in Aquaphor®. The theory is that the cholestyramine binds bile acids that may contribute to perineal dermatitis. There are only case reports supporting the use of this mixture.

Some mixtures for “Butt Paste” contain antifungals (eg, clotrimazole) or different protectants (eg, karaya gum). There is even a commercially available product call Boudreaux’s Butt Paste® that contains boric acid, castor oil, mineral oil, zinc oxide, and peru balsam. Orders written for “Butt Paste” are not valid and will not be dispensed. Zinc oxide ointment is recommended as an alternative.

Other coined terms should also be avoided. A “Banana Bag” is any variation of intravenous dextrose and/or sodium chloride with multiple vitamins, thiamine, folic acid, plus-minus magnesium, and/or potassium. This mixture is also sometimes referred to as a “Rally Bag” or “Rally Pack.” An order for a “Banana Bag” is not a valid order.

“GI Cocktail” is another coined term that can lead to confusion. The typical

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Formulary update, from page 1

Clozapine is an atypical antipsychotic that was requested for addition because of nonformulary use at Shands Vista. Clozapine has not been listed in the *Formulary* because it previously was available only via a limited-distribution program that prohibited it from being stocked in the hospital setting. Now it can be stocked.

Published studies, systematic reviews, and evidence-based guidelines justify the addition of clozapine based on its proven effectiveness. Because of the potential to cause agranulocytosis in 1% of patients (or less), weekly white blood cell counts are required during the first 6 months of treatment. Bi-weekly monitoring is required for the next 6 months, and monitoring is required monthly for patients treated longer than a year. If a patient's white blood cell count decreases below pre-established guidelines, they must stop clozapine and not be rechallenged or risk death.

In addition to the risk of agranulocytosis, clozapine has other potentially serious adverse effects including seizures, cardiomyopathy, and other cardiac and respiratory effects. Clozapine's other common adverse effects include weight gain, hyperglycemia (diabetes), sedation, hypotension, tachycardia, nausea, hyperlipidemia, hypersalivation (especially at night), and sweating.

Hospital policy will assure appropriate monitoring of clozapine before dispensing. In the hospital setting, policies usually require weekly monitoring so that the patient's duration of therapy does not need to be determined.

Current evidence-based guidelines recommend clozapine for treatment-resistant schizophrenia, patients with schizophrenia and suicidal ideation or behavior, and possibly for patients with schizophrenia and assaultive behavior. Because of the potential to cause severe adverse effects, clozapine is only used when patients have failed or cannot tolerate at least 2 other therapies.

The **orally disintegrating clozapine** tablets (Fazaclon[®]) were designated nonformulary and not available.

Glutaraldehyde is a chemical with major uses based on its highly reactive properties that cross-link cellular proteins. In the medical field, glutaraldehyde is used for cold sterilization of surgical equipment and other instruments, like endoscopes. It is also used as a tissue fixative.

Glutaraldehyde 0.6% solution was evaluated for use in toughening tissue allografts used in cardiac surgery and vessel repairs. There are published retrospective series that demonstrate the usefulness of glutaral-

dehyde for atrial and ventricular septal defect (ASD & VSD) repairs. These data suggest that glutaraldehyde improves the durability of these repairs.

However, there are significant safety concerns with this product. Policies will be established for safe preparation, storage, labeling, handling in the operating room (OR), and disposal. The solution will be colored with fluorescein to avoid confusion with other clear solutions. Glutaraldehyde 0.6% will only be delivered from the OR Pharmacy directly to the staff performing the surgery.

Levofloxacin is a third-generation fluoroquinolone. It has been considered a restricted nonformulary drug. This category of drugs is being phased out of the *Formulary* because it implies that a drug is reasonable and available for specific uses but is "nonformulary." This is better described as a formulary agent that is restricted. Thus, the Anti-Infective Subcommittee recommended that this designation be changed. This does not alter the limited manner that levofloxacin will be used at Shands at UF.

Ondansetron is a selective serotonin antiemetic commonly used for chemotherapy-induced and post-operative nausea and vomiting. In January 2000, ondansetron orally disintegrating tablets (ODT) were added in the *Formulary*. Ondansetron oral solid tablets were deleted and the policy of dispensing the ODT for all oral orders was adopted. This decision was made because the ODT dosage form was more versatile and there was no difference in cost. The net effect was a decrease in inventory with a perceived increase in dosing flexibility. The ODT could be used instead of an oral liquid or, in some cases, in place of injectable ondansetron.

Since that decision, there have been 2 complaints. The ODT dosage form is so light, that in some settings the tablets are prone to blowing away. For example, in the Bone Marrow Unit, there have been reports of the ondansetron ODT being blown away in the laminar flow rooms.

Also, some patients cannot tolerate the taste of ondansetron ODT. They complain that the tablets are too sweet, and it exacerbates their nausea and vomiting. These patients were switched to injectable ondansetron.

In order to address these problems, the oral solid tablet was added in the *Formulary* for use in patients who cannot tolerate the ODT.

Estradiol valerate in oil is an intramuscular dosage form of estrogen. It is a very old product that has not been used. It has not been stocked in the Pharmacy for many years, yet is still technically listed in the *Formulary*. Since there are alternatives (eg, injectable conjugated

estrogens), it was removed from the *Formulary*.

Magic Mouthwash is a mixture of medications that has been used to treat mucositis, particularly in patients receiving chemotherapy for cancer. Magic Mouthwash has been listed in the *Formulary*, and the annual formulary review identified this listing as a potential safety risk. Prescribers may not be aware of its constituents.

The magic mouthwash formulation that has been used at Shands at UF consisted of 4 parts nystatin suspension 100,000 units/mL, 3.5 parts diphenhydramine (Benadryl[®]) elixir, and 1 part lidocaine (Xylocaine[®]) viscous 2%. There are other formulations of "Magic Mouthwash" used at other institutions (ie, containing aluminum-magnesium hydroxide [Maalox[®]] and/or corticosteroids). This can be confusing. Patients may be allergic to 1 of the ingredients, which may not be appreciated based on the labeling of the product.

A Cochrane evidence-based review on the interventions for treating oral mucositis in patients with cancer concluded that there was no evidence that Magic Mouthwash is effective. The American Cancer Society (ACS) guidelines for the prevention and treatment of oral mucositis state that there is no significant evidence of the effectiveness or tolerability of any mixture used for mucositis.

Therefore, Magic Mouthwash was removed from the *Formulary*. Saline rinse is recommended as an alternative because there is published evidence that saline mouthwash promotes healing and is equivalent to other products used for mucositis.

Duloxetine is a selective serotonin/norepinephrine reuptake inhibitor (SNRI), like venlafaxine. It has been approved for the treatment of major depressive disorder and painful diabetic neuropathy. Off-label uses of duloxetine include fibromyalgia and urinary incontinence.

Other SSRI and SNRI medications in the *Formulary* include: escitalopram, fluoxetine, paroxetine, sertraline, and venlafaxine. Duloxetine is 20 times more expensive than fluoxetine; 2 times more expensive than escitalopram, paroxetine, or sertraline; and 1.5 times more expensive than venlafaxine.

To evaluate the safety and efficacy of duloxetine, several placebo-controlled trials have been conducted. A comparative study of duloxetine versus paroxetine showed equal efficacy in the treatment of major depressive disorder. Patients receiving duloxetine experienced less sexual
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Formulary update, from page 2 dysfunction when compared to paroxetine and placebo. No other differences were significant between the treatment groups. Venlafaxine and duloxetine have not been compared, and no other head-to-head trials have been conducted.

A randomized, placebo-controlled clinical trial has compared duloxetine to placebo to treat diabetic neuropathy. Treatment with duloxetine 60 mg 1 or 2 times daily improved mean pain scores from baseline. Adverse events increased significantly with the increase in dose of duloxetine.

Based on the lack of sufficient data, duloxetine remains nonformulary at this time.

Myfortic® is an enteric-coated, extended-release, solid oral dosage form of mycophenolic acid. Mycophenolic acid inhibits lymphocyte purine synthesis by inhibiting the rate-limiting enzyme in the de novo pathway for purine synthesis in lymphocytes. It is most often used in combination with cyclosporine or tacrolimus and corticosteroids for the prevention of acute cellular rejection in organ transplantation.

CellCept®, mycophenolate mofetil (MMF), which is currently listed in the *Formulary*, is similar to Myfortic®, enteric-coated mycophenolate sodium (EC-MPS). MMF is a pro-drug of mycophenolic acid, which the liver hydrolyzes to form the active com-

ponent, mycophenolic acid.

EC-MPS was developed with hopes that slower and more distal absorption from the gastrointestinal tract would decrease the occurrence of gastrointestinal adverse effects — most commonly, diarrhea. Unfortunately, this has not been shown in clinical trials, as adverse effects were identical between the MMF and EC-MPS groups.

When dosed using recommended doses for each medication, there appears to be no clinically significant difference between these medications in pharmacokinetic, pharmacodynamic, or clinical parameters. The only comparative pharmacokinetic study between these medications showed no significant difference in maximum concentrations (C_{max}) or total drug exposure (AUC). EC-MPS was shown to have a longer time to maximum concentration (T_{max}). This difference is not expected to contribute to any clinical outcomes. No difference has been shown in clinical outcomes (biopsy proven acute rejection, graft loss, death, or treatment failure) or adverse effects at 6 and 12 months with MMF and EC-MPS as studied in renal transplant patients in 2 randomized controlled trials.

The hope for Myfortic® is that it will have greater gastrointestinal tolerance than mycophenolate mofetil. There are anecdotal instances when patients have been able to switch to Myfortic® and demonstrate better gastrointestinal tolerance, and there are ongoing post-mar-

keting studies on this issue here at UF.

CellCept® is available in a solid oral dosage form, an oral liquid dosage form, and an intravenous dosage form. Myfortic® is available only in a solid oral dosage form.

Myfortic® was not added in the *Formulary*, but will be available via nonformulary request for patients who are already admitted on this product. At this time, there will be no effort to switch patients from Myfortic® to CellCept®.

The criteria for use for **cefepime, ciprofloxacin, and gatifloxacin** were revised to empower the Anti-Infective Stewardship Program (AISP) to streamline therapies. Once culture results are known and/or infection is ruled out, the AISP is authorized to streamline or discontinue cefepime, ciprofloxacin, or gatifloxacin therapy.

These actions will be based on culture and sensitivity results and a thorough clinical review of the patient, which includes discussing the patient with the appropriate service. The AISP is also authorized to stop therapy once a patient has completed an appropriate treatment course.

If there is disagreement with a decision made by the AISP, there is an appeals process. If necessary, the Chief of Staff would ultimately make the decision about the appropriateness of the decision of the AISP. However, there are several interim steps before this would be necessary.

POLICIES AND PROCEDURES

Restricting anti-infectives in “Hospital” clinics

There are several clinics serviced by the inpatient pharmacy services and which are physically located in a “hospital” setting. These clinics have caused some confusion regarding use of restricted anti-infectives.

The P&T Committee voted to restrict anti-infective agents in these clinics as is done in the inpatient units. The purpose of restriction is primarily to prevent the development of resistant organisms. As such, it makes sense to have the same restriction policies based on the physical location of these clinics. Therefore, these restriction policies apply to the following clinics:

- **Outpatient Bone Marrow Transplant Clinic**
- **Burn Clinic**

It is estimated that this should be applicable only a few times each year. Monday through Friday, Infectious Diseases approval will be necessary. On holidays, Saturdays, and Sundays, the anti-infective will be dispensed and then the case referred to the ID Service for follow-up on the next weekday. Approval of restricted anti-infectives for the BMT Clinic will be required on weekends and holidays.

Medication safety, from page 1

GI Cocktail includes liquid antacid (eg, Maalox®), viscous lidocaine, and an anticholinergic (Donnatal®, which is a mixture of atropine, hyoscyamine, scopolamine and phenobarbital). The cocktail is given for chest pain to rule out gastrointestinal problems versus a more serious complaint. Like many of these combinations, the rational of the mixture has been questioned. “GI Cocktail” is not a valid order.

In the past, coined names have been supported by pharmacies. Coined names for mixtures avoid having many different possible formulations, which enables the concoctions to be prepared in advance. Although this is convenient, it may not be safe. If mixtures are used, specifying the specific ingredients and their amounts could help avoid medication errors. Often a single ingredient can be used instead of these mixtures (eg, antacid instead of a GI Cocktail). Magic mouthwash mixtures will no longer be compounded.

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