The Pharmacy and Therapeutics Committee met September 17, 2002. 3 drugs or dosage forms were added in the Formulary and 3 products were deleted. 1 drug was evaluated, but not added.

**ADDED**

- **Abacavir + Lamivudine + Zidovudine**
  (Trizivir® by GlaxoSmithKline)
- **Metoprolol ER**
  (Toprol® XL by AstraZeneca)
- **Ranitidine Tablets**
  (generic and Zantac® by GlaxoSmithKline)

**DELETED**

- **Collagen Implant**
  (Contigen® by Bard)
- **Nizatidine**
  (Axid® by Eli Lilly)*
- **Protirelin**
  (eg, Thyrel® TRH by Ferring Pharmaceuticals)

*designed nonformulary and not available

**EVALUATED, BUT NOT ADDED**

- **Tegaserod**
  (Zelnorm® by Novartis)

Trizivir® is a combination product containing **abacavir** (300 mg), **lamivudine** (150 mg), and **zidovudine** (300 mg). Each of these nucleoside analog reverse transcriptase inhibitors is already listed in the Formulary. Trizivir® was added in the Formulary to facilitate the continuation of outpatient therapy in patients admitted on this drug. It would be unacceptable for patients to miss doses of their antiretroviral therapy when they are admitted to the hospital because a drug is not listed in the Formulary.

When an order is written, there are expectations as to how soon those orders will be carried out. The person writing the order often adds a word to the order to specify the priority of that order. For things that are needed right away, terms like “STAT” or “NOW” or “ASAP” are used. Unfortunately, the definitions for these terms are not widely known. Also, they vary from institution to institution, department to department, and sometimes even from item to item.

Standards for turn-around times need to be established so that expectations can be appropriately set. Also, if departments are not meeting expectations, quality improvement efforts can be undertaken to try to meet these standards.

This article focuses on the turn-around times for drugs, but information on the turn-around times of other frequently ordered things (laboratory results and x-rays) are presented for contrast. Standards for drugs should not be applied to other departments.

The amount of time from the ordering of a drug to its administration can be important—depending on the situation. The delay in the administration of an antibiotic can influence a patient’s ultimate outcome. By contrast, giving orders an inappropriate priority (ie, “Dulcolax STAT”), can dilute the priority of those things that really need to be done right away.

Emergency drugs are in crash carts, which are immediately available for a code. Essentially, there is no turn-around time. No orders are written before these drugs are given. Emergency drugs are administered as they are needed and the documentation occurs concurrently or after the fact.

Emergent medications are available from SureMed® cabinets and can be administered as soon as the order is given. The patient’s nurse has immediate access to the medication without a pharmacist’s review. The P&T Committee establishes the list of drugs that are available without a pharmacist’s review.

There are rational reasons that some drugs should be available without a pharmacist’s review, which could delay therapy. Examples of these situations include when a physician controls the ordering, dispensing, and administering the drug (eg, operating room, endoscopy suite). If a patient’s clinical status would be significantly compromised by a delay resulting from a pharmacist’s review and the increased risk is worth the benefit (eg, pain control), drugs may be approved for the emergent list.

**STAT**-drugs have a turn-around time of 30 minutes. 15 minutes of this time is for nursing processing-administration and 15 minutes is for pharmacy processing and dispensing. When a physician writes a STAT order, it is important that it be given to the ward clerk immediately. The clock starts counting from the time an order is written. A delay in getting the order to a unit clerk or nurse will slow down the process when orders are being faxed to the Pharmacy.

(continued on page 3)
Each component of Trizivir® is available separately. Abacavir (Ziagen®) is also known as ABC; lamivudine (Epivir®) is also known as 3TC; and, zidovudine (Retrovir®) is also known as ZDV. Those patients who use treatment regimens would otherwise include these 3 nucleoside analogues should only use this combination product. Because Trizivir® contains 3 different drugs in the same tablet, it may improve compliance in the ambulatory setting. The recommended dose is 1 tablet twice a day.

Trizivir® may be used alone or in combination with other antiretroviral agents for the treatment of HIV infection. It should not be administered concomitantly with abacavir, lamivudine, or zidovudine.

The sometimes fatal adverse event of hypersensitivity caused by abacavir must be considered. In clinical studies of abacavir, a hypersensitivity reaction has occurred in about 5% of patients. Signs or symptoms of hypersensitivity include fever, skin rash, fatigue, gastrointestinal symptoms, and respiratory symptoms, such as pharyngitis, dyspnea, and cough. Rechallenge is contraindicated after a diagnosis of hypersensitivity has been made. Neither Ziagen® nor Trizivir® should be taken by someone who may have experienced symptoms of a hypersensitivity reaction to abacavir.

Other possible side effects include lactic acidosis, severe liver problems, anemia, neutropenia, nausea, fatigue, and myopathy.

Toprol® XL is an extended-release metoprolol. It has been frequently prescribed nonformulary. Toprol® XL is also listed in the top 50 prescribed drugs in the US.

Metoprolol is a beta-1-selective receptor antagonist. Metoprolol is used for hypertension, heart failure, and post-myocardial infarction. Toprol® XL is given once a day, while regular-release metoprolol is given twice a day for most indications.

Metoprolol ER has been shown to decrease mortality and hospitalization in the patients with NYHA Class II through IV heart failure in the MERIT-HF study. The dosage forms of Toprol® XL allow for titration of doses in heart failure patients started on metoprolol. Toprol® XL is less expensive that carvedilol (Coreg®), which is another beta-blocker with some alpha-blocking activity listed in the Formulary and which is used to treat patients with heart failure. (See table on page 3.)

Ranitidine tablets replaced nizatidine capsules as the oral solid H2-blocker in the Formulary in September. This change results in ranitidine being the sole H2-blocker listed for injection, liquid, and oral solid use.

In January 1995, H2-blockers were deemed therapeutically equivalent. In April 1995, nizatidine was added in the Formulary. Since then, all orders for oral solid H2-blockers have been changed to nizatidine. The low price that we have received for nizatidine for the last 7 years stopped when generic versions of nizatidine were approved.

Ranitidine was selected as the oral solid H2-blocker replacement for nizatidine based on cost and convenience. Ranitidine granules and syrup have been used as oral liquid H2-blockers, so ranitidine oral solid is consistent with this option. We also use injectable ranitidine. Nizatidine does not come as an oral liquid.

Orders for nizatidine 150 mg twice a day will be automatically converted to ranitidine 150 mg twice a day. Orders for famotidine 20 mg twice a day also will be converted to ranitidine 150 mg twice a day. Nizatidine is now nonformulary and not available like famotidine.

Contigen® is a sterile, nonpyrogenic collagen implant device that is injected into the tissues around a patient’s urethra to treat urinary incontinence caused by urinary sphincter deficiency. It is an alternative to other procedures (eg, urinary sphincter replacement surgery).

Although a device, Contigen® was added in the Formulary because it “looks” like a drug. It is available as a syringe and must be stored in a refrigerator. It was deleted from the Formulary because of lack of use.

Protirelin® was a synthetic peptide identical to endogenous thyrotropin-releasing hormone (TRH). It had a labeled indication as an adjunctive agent in the diagnostic assessment of thyroid function. It was used as an adjunct to other diagnostic procedures to diagnose pituitary or hypothalamic dysfunction.

In practice, the response to TRH in hypothyroid and pituitary disease overlap and this test is no longer used. Ferring discontinued the manufacturing of protirelin.

Tegaserod is a recently approved drug for irritable bowel syndrome (IBS). IBS is a common disorder. Recent research suggests that neurotransmitters are involved in the pathogenesis of IBS. Treatment depends on the predominant IBS symptom. Constipation-predominant IBS has been managed with fiber and osmotic laxatives, but tegaserod is a new therapeutic option. Tegaserod is the only drug in the US with a labeled indication for constipation-predominant IBS.

Tegaserod stimulates Type-4 serotonin receptors, which are thought to trigger the release of other neurotransmitters that stimulate intestinal peristalsis and secretion. Zelnorm®’s labeled indication is for the short-term treatment of women with IBS whose primary bowel symptom is constipation. The labeled dosage is 6 mg twice a day before meals for 4 to 6 weeks. Responders may receive an additional 4 to 6 weeks. The safety and efficacy of tegaserod in men and children has not been established.

The quality of the published evidence for the treatment of IBS is not good. Defining and measuring the appropriate response variables for IBS is difficult. Currently, there is insufficient published evidence to support the addition of tegaserod in the Formulary. Formulary consideration was tabled for 12 months. Since tegaserod will remain nonformulary, sales representatives cannot promote it to the housestaff.

There were few common adverse effects associated with the use of tegaserod in clinical trials. Diarrhea and headache occurred most frequently. Diarrhea is an extension of the pharmacology of tegaserod and can decrease with time. As with all new therapies, there may be rare but serious adverse effects that have not yet been identified.

The FDA approved tegaserod in July 2002. FDA approval came approximately 1 year after it was rejected because of safety concerns. There was a higher rate of gall bladder surgeries and other abdominal and pelvic surgeries in tegaserod-treated patients. The FDA used safety data from other countries where tegaserod was already marketed and a commitment for a post-marketing cohort safety trial to approve tegaserod.

There are some other concerns about tegaserod. The limited available data suggest that the treatment effect in IBS is small and that effectiveness appears to decrease with time. Since IBS is a chronic condition, this appears to be a problem. Tegaserod is expensive and the role of this agent in the inpatient setting is unclear. Off-labeled use of tegaserod (ie, chronic constipation, the prevention of postoperative ileus) is a potential problem. There are no published data to support these off-labeled uses.
Why are drug prices unpredictable?

Drug pricing is complicated. Large increases in drug costs, government intervention, and market dynamics create a system that is difficult to follow, particularly for prescribers attempting to use cost-effective drug therapy.

What pharmacies pay for drugs is not uniform. The Average Wholesale Price (AWP) is the usual published price for pharmaceuticals seen in publications like The Medical Letter. While the AWP is useful for a rough comparison between drugs, most pharmacies pay less than AWP. The real or acquisition cost depends on many factors.

Hospitals use their formularies to negotiate prices. A formulary is a list of drugs approved by a Pharmacy and Therapeutics Committee for use in a hospital, HMO, or another health system. Inexpensive generic drugs are usually listed in formularies, when they are available.

One technique that hospitals use to lower the costs of drugs that are not generically equivalent is to deem them therapeutically equivalent. By bidding brand name drugs that are deemed therapeutically equivalent by a P&T Committee, drug costs decrease. As with H2-blockers (discussed in this issue of the Bulletin), a low-cost agent is the only choice listed in a formulary.

Drug costs in a formulary system are often less than that paid by a community pharmacy. This difference is why hospital outpatient pharmacies cannot legally fill prescriptions for the general public with drugs purchased for inpatient use.

This can create confusion when prescribing discharge medications. At Shands, Toprol® XL is inexpensive. However, it is more expensive in the community setting.

Acquisition costs do not always predict what patients pay. The charge is often based on AWP, which is higher than the acquisition cost. Some large pharmacies may charge less than they pay for a drug to attract customers for the other things they sell. Charges can vary dramatically between pharmacies. (See table.)

Encouraging cost-conscious patients to “shop around” for the best prices may seem to make sense, but it may compromise patient care. Pharmacists are unable to detect drug-related problems (eg, interacting drugs prescribed by different physicians) without a complete drug profile.

Patients generally pay a co-pay, which is a portion of the total cost of their prescription. Many HMOs and insurance companies charge a larger co-pay for brand name products that are available as generics. Patients who pay the full price of their prescriptions (eg, elderly patients on Medicare without supplement insurance) may be better off with a slightly less optimal generic drug that they can afford, rather than an expensive drug that they will not be compliant with.

Here are a few points to remember when prescribing drugs.

- Costs are not uniform and the terms cost and charge are not interchangeable. A drug that is inexpensive in the hospital is not necessarily the least expensive agent for patients to purchase in the community.
- Knowing that a patient has Medicaid or insurance that requires only a small co-pay should not exempt prescribers from using the least expensive product that will adequately and safely treat a patient. We all pay for unnecessary, expensive therapies through taxes and rising insurance premiums. Ask pharmacists for comparative costs of the frequently prescribed drugs and compare them to other agents.
- For most medical conditions, generic drugs save money for patients and the healthcare system. Generic drugs in a class are usually in most formularies and are the least expensive alternatives.

By Bill Harbilas, PharmD

### TABLE: COSTS OF A MONTH’S SUPPLY OF BETA-BLOCKERS

<table>
<thead>
<tr>
<th></th>
<th>Metoprolol (generic)</th>
<th>Toprol® XL</th>
<th>Coreg®</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50 mg PO BID</td>
<td>100 mg PO QD</td>
<td>25 mg PO BID</td>
</tr>
<tr>
<td><strong>Average Wholesale Price</strong></td>
<td>$32.66</td>
<td>$32.72</td>
<td>$103.34</td>
</tr>
<tr>
<td><strong>Shands Inpatient</strong></td>
<td>$3.60</td>
<td>$1.20</td>
<td>$78.00</td>
</tr>
<tr>
<td><strong>Large Chain #1</strong></td>
<td>$15.99</td>
<td>$35.79</td>
<td>$111.89</td>
</tr>
<tr>
<td><strong>Large Chain #2</strong></td>
<td>$18.49</td>
<td>$38.69</td>
<td>$110.79</td>
</tr>
<tr>
<td><strong>Shands Outpatient</strong></td>
<td>$16.27</td>
<td>$33.95</td>
<td>$97.51</td>
</tr>
<tr>
<td><strong>Supermarket Pharmacy</strong></td>
<td>$14.95</td>
<td>$35.95</td>
<td>$114.95</td>
</tr>
</tbody>
</table>

### TABLE: TURN AROUND TIME COMPARISON

<table>
<thead>
<tr>
<th></th>
<th>Drug</th>
<th>Labs</th>
<th>X-Rays</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Emergency</strong></td>
<td>0h</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Emergent</strong></td>
<td>0h</td>
<td>15 min</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Urgent</strong></td>
<td>NA</td>
<td>30 min</td>
<td>NA</td>
</tr>
<tr>
<td><strong>STAT</strong></td>
<td>30 min</td>
<td>2 hrs</td>
<td>≤ 1 hr</td>
</tr>
<tr>
<td><strong>Now</strong></td>
<td>60 min</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>ASAP</strong></td>
<td>NA</td>
<td>2 hrs</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Routine</strong></td>
<td>2 hrs</td>
<td>4–8 hrs</td>
<td>≤ 8 hrs</td>
</tr>
</tbody>
</table>

NA = not applicable: this term not used by this department

a Immediately available in the crash cart for codes

b Immediately available in SureMed® cabinets without pharmacist approval (eg, pain meds)

c Blood Bank Only

d Limited to tests for certain conditions

e 45 minutes for Blood Bank only

f Based on time from receipt in the laboratory to posting in HIS

g Only applies to routine procedures
SHORTAGES

Is there an influenza vaccine shortage this year?

Shortages of pharmaceuticals continue to be a major problem. Last year, a delay in the shipment of influenza vaccines left many healthcare professionals and patients scrambling to find an adequate supply. There has been concern expressed about the supply for this year. Fortunately, there is no shortage of influenza vaccine this year. Manufacturers will supply about 94 million doses of vaccine for the 2002-03 season. The supply will be somewhat delayed again this year.

For example, the first shipment of 25% of Shands’ allotment of influenza vaccine was received in September. Another 25% is expected by the end of October. Shands will not receive its full allotment for the year until November. Healthcare providers should keep this in mind as they begin to vaccinate their patients in the ambulatory setting.

On March 6, 2002, the FDA Vaccines and Related Biologicals Products Advisory Committee made recommendations for the influenza virus strains to be included in the 2002-03 influenza vaccine. The 2002-2003 trivalent vaccine will consist of H1N1, A/New Caledonia/20/99; H3N2, A/Panama/2007/99 (an A/Moscow/10/99-like virus); and, B/Hong Kong/330/2001-like virus strain. These are the same strains earlier recommended by the World Health Organization.

Because the supply of influenza vaccine will be staggered, people with the highest risks from influenza should be vaccinated first. People at high risk of complications from influenza include: people 65 years old or older; residents of nursing homes and other chronic-care facilities that care for people of any age who have chronic medical conditions; adults and children having chronic disorders of the pulmonary or cardiovascular systems, including asthma; adults and children who have had medical treatment or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus); children and teenagers, 6 months to 18 years old, receiving long-term aspirin therapy (who could develop Reyes syndrome after influenza infection); and, women in the second or third trimester of pregnancy during the influenza season.

People who can transmit influenza to people at high risk include: physicians, nurses, and other personnel in both hospitals and outpatient-care settings, including emergency response workers; employees of nursing homes and chronic-care facilities who have contact with patients or residents; employees of assisted living and other residences for people in high-risk groups; people who provide home care to people in high-risk groups; and, household members, including children, living with people in high-risk groups. Healthcare professionals should be vaccinated at the same time as high-risk patients.

Even patients who are not high-risk benefit from vaccination as they can avoid influenza, miss fewer days from work, and have less need for medical visits and medication, including antibiotics. When the supply of influenza vaccine is more plentiful, special effort should be made to vaccinate children who live with household members who are in high-risk categories. Watch for information from Occupational Health Services about its plan to vaccinate hospital employees, which will begin October 10, 2002.