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SHANDS at the University of Florida

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Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met February 15, 2005. 7 drugs were added in the *Formulary* and 5 drugs were deleted. 2 drugs were evaluated and not added. Criteria for use were changed for 1 drug.

◆ ADDED

Ampicillin-Sulbactam (Unasyn® by Pfizer)*

Atomoxetine (Strattera® by Eli Lilly)

Dalfopristin-Quinupristin (Synercid® by Monarch Pharmaceuticals)*

Dichlorotetrafluroethane-Ethyl Chloride (Fluro-Ethyl® by Gebauer)

Hetastarch in Lactated Ringers (Hextend® by Hospira)

Immune Globulin, Intravenous (Gamunex® by Bayer)**

Secretin, Human (ChiRhoStim® by ChiRhoClin)

**Restricted to Infectious Diseases Approval or the Anti-Infective Stewardship*

***Restricted*

◆ DELETED

Diazoxide Injection (Hyperstat® by Schering)***

Ethyl Chloride (Ethyl Chloride)***

Hetastarch in Normal Saline (Hespan® by Bristol Myers Squibb)***

Secretin, Porcine (Secreflo® by Repligen)***

Streptokinase (Streptase® by AstraZeneca)***

****Nonformulary and Not Available*

(continued on next page)

NEWS

Finally, some quality inside the "Bulletin"

Readers will notice a change beginning with this issue of the *Drugs & Therapy Bulletin*. A "newsletter-inside-a-newsletter" concept begins this month.

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The *Clinical Practice Bulletin* has been "inserted" inside the *Drugs & Therapy Bulletin* because both publications have similar target audiences and purposes. The *Clinical Practice Bulletin* covers clinical practice issues and the Academic Quality Support Agreement.

Dr. Patrick Antonelli has written an article in the first issue of the *Clinical Practice Bulletin* that explains the purpose of the Clinical Practice Committee and the content that will be in this newsletter. Although quality medical care is one of their focuses, there is much more that just quality issues inside both bulletins.

Eventually, the *Clinical Practice Bulletin* may spin-off and become a stand-alone publication. For now, look for the insert with important information about clinical practice issues.

The *Drugs & Therapy Bulletin* is affiliated with the Pharmacy and Therapeutics (P&T) Committee. Like the Clinical Practice Committee, the P&T Committee is a medical staff committee. The P&T Committee is the formal line of communication between the medical staff and Shands at UF regarding all drug related matters. Both bulletins are intended to get information from these important medical staff committees to the medical staff they affect.

Thus, the main targets for both newsletters are the medical staff. Both publications, however, contain information that will interest other hospital staff (eg, nurses, pharmacists, ward clerks). Nurse managers and department heads that get these newsletters are encouraged to post these newsletters in your areas for your staff. When there are issues that are relevant, please review them with you staff. Both bulletins will be available on the Shands intranet.

The *Clinical Practice Bulletin* covers clinical practice issues and the Academic Quality Support Agreement (AQSA). Some of these issues overlap with topics that are discussed at the P&T Committee. For example, the last 2 issues of the *Drugs & Therapy Bulletin* contained articles about inappropriate abbreviations. Since this is part of the AQSA, articles on this topic could appear in either bulletin.

If names needed to be added or deleted from the mailing list for the bulletins, please send this information to Editor, *Drugs & Therapy Bulletin,* PO Box 100316. If you have editorial comments about the *Drugs & Therapy Bulletin,* they can be e-mailed to hatton@ufl.edu. For comments about the *Clinical Practice Bulletin,* please send you comments to mookel@shands.ufl.edu.

INSIDE THIS ISSUE

Formulary update, *from page 1*

◆ EVALUATED, BUT NOT ADDED

Glycerin, Sterile, Compounded
(Glycerol)

Pegvisomant
(Somavert® by Pfizer)

◆ CRITERIA FOR USE CHANGE

Imipenem-Cilastatin
(Primaxin® by Merck)

Ampicillin-sulbactam injection is a combination of a penicillin (ampicillin) and a beta-lactamase inhibitor similar to Timentin® (ticarcillin + clavulanate) and Zosyn® (piperacillin + tazobactam). These antibiotic combinations have a broad spectrum of activity against aerobic and anaerobic bacteria. Compared with Timentin® and Zosyn®, Unasyn® has less antipseudomonal activity. Unasyn® does cover Enterococcus species.

In June 2003, Unasyn® was designated "not available" because it was rarely used. It was thought that other alternatives could be used. Unasyn® was re-evaluated by the Anti-Infective Subcommittee as part of the Surgical Infection Prophylaxis (SIP) initiative.

Unasyn® was determined to be a reasonable agent for surgical prophylaxis for complicated biliary surgeries. Further, it is used as an alternative agent for skin and soft tissue infections, community-acquired intra-abdominal infections, and gynecological infections. Unasyn® is restricted to approval by the Infectious Diseases Service or the Anti-Infective Stewardship.

Atomoxetine is a nonstimulant, noncontrolled prescription alternative to stimulants for the treatment of attention-deficit hyperactivity disorder (ADHD). It has labeled indications for ADHD in children and adults. Although the mechanism of action is unknown, it is presumed to be associated with increased central norepinephrine by inhibition of presynaptic norepinephrine transporters.

Atomoxetine's effect on norepinephrine is associated with its common adverse effects. Increased blood pressure and heart rate may occur, so it should be used with caution in patients with hypertension or other cardiovascular diseases. Atomoxetine is contraindicated in narrow angle glaucoma. It may decrease appetite; therefore, growth in children must be monitored.

Recently, the FDA added a bolded-warning to atomoxetine's label about possible hepatotoxicity, which may progress to liver failure and death or need for a liver transplant. Liver function monitoring is recommended.

Atomoxetine has been shown to be more effective than placebo in clinical trials. In the limited published data that have been published, atomoxetine has been shown to be equal to stimulants for ADHD. However, recent abstracts suggest that stimulants may be more effective.

Patients are often admitted for inpatient care receiving atomoxetine, especially at Shands at Vista. In the outpatient setting, atomoxetine is being used in patients who do not tolerate stimulants or have other objections to stimulant use (eg, prefer a noncontrolled substance). Atomoxetine was added in the *Formulary* for continuity of care for the treatment of ADHD.

Dalfopristin-quinupristin is an injectable antibiotic used for the treatment of infections caused by resistant gram-positive organisms. Synercid® was deleted from the *Formulary* in October 2003 because of its perceived deficiencies (ie, holes in its antibacterial spectrum [Enterococcus faecalis] and serious toxicities [eg, bone marrow suppression]). At that time, Synercid® was considered obsolete. Since then there have been infections that could not be treated with alternatives like linezolid or daptomycin because of resistance or adverse effects.

The Anti-Infective Subcommittee recommended that Synercid® be re-added in the *Formulary* as an alternative for the treatment of resistant, gram-positive cocci infections. The use of Synercid®, which is expected to be very infrequent, is restricted to the approval of the Infectious Diseases Service or the Anti-Infective Stewardship.

Dichlorotetrafluroethane-ethyl chloride is a nonflammable alternative to **ethyl chloride.** Both are vapocoolants used to "freeze" a topical area and relieve pain from minor procedures and some types of injuries. Fluro-Ethyl® was added to replace ethyl chloride because it is safer and has less restrictive storage requirements. Flammable liquids, like ethyl chloride, require special storage, making their use impractical.

Fluro-Ethyl® has a very low boiling point. When sprayed onto the skin, it rapidly evaporates, producing an intense cold. It should be used only for external use and it should not be used on patients' extremities if they have vascular impairment.

Hetastarch in lactated ringers (LR) solution was added in the *Formulary,* while **hetastarch in normal saline (NS)** was deleted. This change will be implemented April 1, 2005. To avoid confusion, only hetastarch in LR will be available.

Hetastarch is an artificial non-protein colloid derived from amylopectin. When administered as an intravenous solution, it acts as a volume expander. The degree of volume expansion and improvements in hemodynamics depend on an individual patient's status. It has a labeled indication for the treatment of hypovolemia when plasma expansion is desired. It is an alternative to crystalloids (eg, normal saline or lactated ringers), other colloids (eg, albumin), or blood.

Hetastarch particles have a wide range of molecular weights. The high-molecular-weight products available in the United States have been associated with bleeding complications. There is some evidence that the risk of bleeding is less with hetastarch in LR instead of hetastarch in NS.

Patients receiving hetastarch in NS may develop hyperchloremic metabolic acidosis. Hetastarch in LR also has shown less effect on biochemical markers for bleeding, and less blood loss has been measured compared with hetastarch in NS in clinical trials. However, the units of blood used was not different between patients receiving hetastarch in LR or NS.

Although current evidence does not prove that hetastarch in LR is superior to hetastarch in NS, these 2 products are at least similarly effective. They are similarly priced. Some clinicians are willing to use hetastarch in LR instead of albumin as a volume expander. Hetastarch in LR cost roughly 50% the cost of albumin.

Therefore, hetastarch in LR was added as a less expensive option to albumin. Hetastarch in LR is should not be used in patients with oliguria or anuria unless it is related to hypovolemia. Due to the potassium in LR, hetastarch in LR should be used cautiously in patients with renal failure or when potassium retention is an issue. Also, it should be used with caution in metabolic or respiratory acidosis or other conditions that have difficulty handling lactate.

Gamunex® is the third brand of **intravenous immune globulin** (IVIG) available at Shands at UF. It was added to Panglobulin® NF and Polygam® S/D, which are IVIGs already listed in the *Formulary.*

IVIGs are primarily IgG immune globulins collected from the plasma of blood donors. They all undergo at least 2 methods for viral depletion and inactivation. There have been no recent cases of viral transmission by IVIG, but all products carry a warning about potential viral transmission and Creutzfeldt-Jakob disease.

(continued on next page)

Formulary update, *from page 2*

IVIGs are used for a variety of indications ranging from supplementation for patients deficient in endogenous immune globulins (ie, primary immunodeficiencies) to a number of autoimmune diseases that may benefit from blocking antibodies and the resultant immunosuppressive effect (eg, immune thrombocytopenic purpura and Kawasaki disease).

Because IVIG is a byproduct of blood donation and plasma processing, it is a limited commodity. There have been periodic shortages of IVIGs. After Shands' allocations of Panglobulin® and Polygam® were cut for 2005, an additional IVIG product was needed in order to assure an adequate supply.

Shands' largest allocation of IVIG is Panglobulin®. This will continue to be the primary product used. Orders written for "IVIG" will be filled with Panglobulin®.

Polygam® will be reserved as much as possible for patients who are sensitive to IgA. Although IVIGs contain IgG, there can be a small amount of "contamination" with IgA and IgM. The amount of IgA varies from brand to brand. Some patients are sensitive to IgA and require a "low-IgA" IVIG. Polygam® has the lowest IgA content and is reserved for these patients. When a specific brand is needed, the order must be specific.

Acute renal failure has been reported in patients receiving IVIG, particularly in patients with impaired renal function who received products containing sucrose. Sucrose is included in some IVIG products as a stabilizer. Large loads of sucrose may damage the renal tubule. Sucrose-free IVIGs that use other stabilizers may be preferable in patients at risk for acute renal failure.

Polygam® remains the primary sucrose-free IVIG listed in the *Formulary.* It uses dextrose as a stabilizer. However, since we have a limited supply of this product and some product needs to be reserved for IgA-sensitive patients, Gamunex® was added in the *Formulary.*

Gamunex® does not contain sucrose as a stabilizer. It contains no sugar and is stabilized with glycine. Although Gamunex® contains less IgA contaminant than Panglobulin®, it is still not considered an acceptable product for patients with IgA sensitivity.

Gamunex® is restricted to patients who need a sucrose-free product when our supplies of Polygam® have been depleted. Gamunex® costs 80% more than Polygam®.

Synthetic **human secretin** will now replace synthetic **bovine secretin** in the *Formulary.* Secretin is a gastrointestinal hormone that is normally released to stimulate the pancreas to aid in food digestion. Exogenous secretin is used for the secretin stimulation test for the diagnosis of chronic pancreatitis.

Porcine secretin was deleted from the *Formulary* in 2001 when the manufacturer discontinued the product. Synthetic bovine secretin was added in the *Formulary* in 2003. Synthetic human secretin now replaces bovine secretin.

A study done here at the University of Florida shows that synthetic bovine and human secretin are equivalent and can be used interchangeably. Both cost the same. The decision to change was made based on physician preference and reports that bovine synthetic secretin might be removed from the market.

Diazoxide injection is a peripheral vasodilator that has traditionally been used to treat hypertensive emergencies. It was deleted from the *Formulary* because of lack of use and the availability of better therapeutic options.

Streptokinase is a thrombolytic agent that has been used to dissolve venous and arterial thrombi. Recently, the manufacturer of streptokinase stopped making this product, necessitating its removal from the *Formulary.* Once our limited supplies have been exhausted, we will no longer be able to provide streptokinase.

Several other thrombolytics are still listed in the *Formulary* including alteplase, tenecteplase, and urokinase. The preferred alternative will depend on the reason for thrombolysis.

Sterile anhydrous glycerin (glycerol) was evaluated for use in chemical rhizotomies, which are used for nerve ablations in the treatment of trigeminal neuralgia. The cause of trigeminal neuralgia is believed to be arterial compression of the trigeminal nerve. When medical therapy fails and microvascular surgical decompression is not a viable option, percutaneous nerve ablation procedures are an alternative.

Sterile anhydrous glycerin is injected around the trigeminal nerve root and ganglion damaging the nerve, which blocks pain signals. Glycerol injection is an alternative to radiofrequency ablation of the nerve.

Since there is no commercially available source of sterile anhydrous glycerol for use in doing rhizotomies, it cannot be added in the *Formulary.* We have contracted with an outside compounding pharmacy that meets our quality standards (eg, end-product testing for content, sterility, and pyrogens). Sterile glycerol can be obtained for an individual patient only with a prescription. Therefore, it will not be listed in the *Formulary,* and a policy for procurement has been established.

Pegvisomant is an analog of human growth hormone that binds to growth hormone receptors on cell surfaces and blocks the actions of endogenous human growth hormone. Pegvisomant has a labeled indication for the treatment of acromegaly in patients who have an inadequate response to surgery and/or radiation therapy and/or other medical therapies or for whom these therapies are not appropriate.

Somavert® is provided to registered patients only through a limited distribution program (ie, the Pfizer Bridge Program). It is not possible for Shands at UF to obtain this product; therefore, it cannot be listed in the *Formulary.*

Patients have been admitted to the hospital taking this product. Since it is available only by a limited distribution program, policy allows patients to use their own supply of this injectable nonformulary drug. Pegvisomant is administered daily by a subcutaneous injection.

Pegvisomant was designated a high-priority nonformulary drug so that pharmacists will immediately notify prescribers that the patient must provide their own supply.

Imipenem-cilastatin is a broad-spectrum antibiotic that has been listed in the *Formulary* for many years. The Shands at UF criteria for use include infections caused by multi-drug resistant gram-negative organisms, necrotizing pancreatitis, and for failure of primary therapy.

Pseudomonas aeruginosa's sensitivity to imipenem is only 82%. *Pseudomonas aeruginosa* is the second most common gram-negative organism isolated at Shands at UF. In order to protect the utility of this agent, prudent use of imipenem is required. Also, resistance to imipenem is conferred to other unrelated antibiotic classes.

A recent audit found that only 52% of patients treated with imipenem for more than 72 hours received it for an appropriate indication. Of the 48% considered inappropriate, 75% were modified based on Anti-Infective Stewardship recommendations and the rest were continued despite the intervention. Continued inappropriate use contributes to gram-negative resistance. Therefore, imipenem use will now be restricted to Infectious Diseases or Anti-Infective Stewardship approval.

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ANTI-INFECTIVE STEWARDSHIP

Vancomycin use will require pre-approval

The P&T Committee approved a 6-month pilot program that will require the pre-approval of vancomycin before it can be prescribed for empiric or therapeutic use. Prophylactic use of vancomycin in an approved surgical infection prophylaxis protocol will not require pre-approval.

This policy was approved after months of interventions by the Anti-Infective Stewardship (AIS) have resulted in some improvements in vancomycin use. Unfortunately, there continues to be significant misuse of vancomycin.

Although patients' vancomycin therapy is often stopped before 72 hours, many patients should not have received treatment in the first place. Exposure to vancomycin can increase a patient's chances of colonization with vancomycin-resistant enterococcus (VRE).

While vancomycin use has stabilized at comparable hospitals, its use continues to increase at Shands at UF despite the AIS's interventions. The incidence of VRE also continues to increase.

The AIS was started in May 2004 after the Medical Executive Committee recommended that mechanisms be developed for antimicrobial evaluation and regulation at Shands at UF. The increasing incidence of infections with antibiotic-resistant organisms and the associated morbidity, mortality, and costs stimulated this action. Increased use and prolonged exposure to antibiotics are factors driving the development of resistance. The goals of the AIS are to slow or decrease the development of resistance and to decrease nosocomial infections.

Vancomycin was one of the first major antibiotics targeted because of the existence of national standards for use (ie, the CDC criteria) and the increasing development of VRE.

Vancomycin was one of the first major antibiotics targeted because of the existence of national standards for use (ie, the CDC criteria) and the increasing development of VRE. The incidence of VRE at Shands at UF has increased from the 1 case in 1993 to over 200 cases per year in 2004.

VRE infections are difficult to treat. VRE colonization is problematic because it can ultimately lead to infection and it makes patient handling more difficult. Nursing care for these patients is much more challenging. Hospitalized patients require isolation, and patients requiring nursing home care are difficult to place. This prolongs length-of-stay, is time-consuming, and can be very expensive.

Before the vancomycin pre-approval program is implemented, the AIS will be meeting with many of the medical departments and divisions. After the educational phase and the pre-approval procedure is implemented, further details will be published in a future issue of the *Drugs & Therapy Bulletin.*