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Drugs & Therapy BULLETIN

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met Aptil 15, 2003. 4 drugs or dosage forms were added in the *Formulary*. 4 drugs or dosage forms were deleted and 4 products were designated not available.

◆ ADDED

Budesonide inhalation suspension*
(Pulmicort Respules® by Astra Zenneca)

**restricted to children less than 9 years old on a general ward in whom an MDI and a spacer is not a viable option*

Nicardipine injection**
(Cardene® by Wyeth Ayerst)

***restricted to the PICU for patients with renal dysfunction and a central line who have failed labetalol*

Saquinavir (Invirase® by Roche)

Tizanidine
(Zanaflex® and generics)

◆ DELETED

Candida skin test
(eg, Candin® by Allermed)***

Chloramphenicol ophthalmic solution (generic)

Mumps skin test
(MSTA® by Connaught)***

Tetanus toxoid skin test
(compounded)***

****also nonformulary and not available*

◆ NONFORMULARY AND NOT AVAILABLE

Inamrinone (eg, Inocor® by Sanofi Synthelabo)

(continued on next page)

POLICIES AND PROCEDURES

Comfort medication during procedures

When an order is written to insert an intravenous catheter, give an intramuscular injection, place an enteral feeding tube, or insert a urinary catheter, the medications needed to prevent discomfort are not usually explicitly ordered. In order to promote good pain management, the P&T Committee has approved a nursing policy that will allow the use of topical and intradermal anesthetics without an explicit order. This will provide pain relief and diminish anxiety associated with these common procedures.

The treating nurse can use ELAMax® (lidocaine 4% cream), EMLA® (lidocaine-prilocaine cream), or a 1% lidocaine intradermal injection to decrease the discomfort of inserting an intravenous catheter or giving an IM injection. Lidocaine gel can be used to facilitate the placement of an enteral tube (eg, NG, NJ, or GT tube). Lidocaine gel can also be used for a urinary catheter placement. The order for the procedure now gives implicit approval to use these products.

The treating nurse will assess the patient for the need for the local anesthetic and determine whether a comfort medication would be helpful. The patient's history of allergies will be reviewed before using a comfort medication. The medication used will be documented in the procedure note or on the medication administration record (MAR). The note will state "per Procedural Comfort Protocol."

DRUG USE EVALUATION

Meperidine use improves...

In May 2002 oral and PCA meperidine were deleted from the *Formulary* and made "not available." Criteria for use for injectable meperidine were developed that limited meperidine use to the treatment of rigors and for analgesia and sedation during short procedures. These decisions were made based on the recommendations of the Pain Committee.

Meperidine is so short-acting that it has to be dosed too frequently for routine pain use. Also, it has a neuroexcitatory metabolite that can cause seizures — even in patients with normal renal function. There are better options for the management of pain. Thus, meperidine PCA and oral tablets were deemed "unavailable."

Injectable meperidine is still listed in the *Formulary* for use in short procedures. A recent audit shows that the use of injectable meperidine has dropped dramatically. These data support successful implementation of the Pain Committee's recommendations.

Physicians still using meperidine will be sent a letter reminding them of the appropriate use of meperidine. Meperidine should be limited to the treatment of rigors and as an analgesic and sedative for short procedures. The Pain Committee's guidelines for the management of pain in adults (http://intranet.shands.org/pharm/pain/AdultPainGuide.pdf) and children (http://intranet.shands.org/pharm/pain/PedsPainGuide.pdf) can be found on the Shands intranet.

INSIDE THIS ISSUE

Formulary, *from page 1*

Budesonide inhalation suspension is a corticosteroid that is inhaled orally for the treatment of chronic stable asthma in children. It was reviewed because of its frequent nonformulary use.

Budesonide suspension is the only commercially available inhaled corticosteroid in a dosage form ready for nebulization. It is an alternative to metered-dose inhaler (MDI) corticosteroids. Fluticasone MDI is listed in the *Formulary.*

There are disadvantages of budesonide inhalation suspension (budesonide nebs) compared with inhaled fluticasone. Budesonide nebs have a longer administration time (ie, 15 minutes versus a few minutes). Budesonide administration requires the time of a respiratory therapist. Also, a special administration device (ie, Pari-LC-Jet nebulizer) must be used or the corticosteroid is not delivered to the lungs. This device costs about $12 and can only be used for 1 patient.

There are few comparative data for budesonide nebs versus inhaled corticosteroids with a spacer device. A study in adults suggested that fluticasone with a spacer was more effective than budesonide nebs. The validity of this study is questionable, however, since most inhaled budesonide is for children. The only labeled indication for budesonide nebs is for children less than 9 years old.

The Pediatric Pulmonary Division supports restrictions for budesonide nebs. It will be limited to patients who are 8 years old or less, on a general pediatric floor (ie, not in an intensive care unit), and for whom Pediatric Pulmonary has established that a MDI corticosteroid and a spacer is not a viable option.

Budesonide nebs are not needed in ICUs because in this setting patients should be receiving a systemic corticosteroid. Budesonide nebs are for stable asthma only. Budesonide nebs are not recommended as a first-line therapy. A corticosteroid MDI plus a spacer is preferred. The Pediatric Pulmonary Division has volunteered to determine if a MDI with a spacer is not a viable option. Budesonide nebs will not be available for use in adults.

Nicardipine injection was evaluated because it is a high-priority nonformulary drug. If requested nonformulary, a significant delay in acquisition would be unacceptable. Although use has been small, it has been occasionally used for pediatric patients in the PICU.

When nicardipine was reviewed in 1997 for post-operative hypertension, it was not added in the *Formulary* because it was determined to be equal to nitroprusside in terms of efficacy, but was 30-times more expensive. This review focused on the pediatric use of injectable nicardipine.

The use of intravenous nicardipine in children has limited published information. There are several case reports and case series using intravenous nicardipine for hypertensive emergencies. There are no randomized, clinical trials that compare nicardipine and other therapeutic options (eg, nitroprusside, labetalol). The reviews that recommend the use of nicardipine base their recommendations on the theoretical risk of thiocyanate toxicity with nitroprusside or the perceived limitation of using a beta-blocker in patients with asthma.

There is no high-quality evidence published on the use of any drug in pediatric patients for the treatment of hypertensive urgencies and emergencies. There are few reports of thiocyanate toxicity with the use of nitroprusside in children with renal dysfunction, and the consensus in the literature is to not use nitroprusside in these patients.

The successful use of labetalol in patients with reversible airway disease has been documented, however. Therefore, labetalol is a reasonable therapeutic option, even if patients have a history of reactive airway disease.

Nicardipine injection was added in the *Formulary* and restricted to use in the PICU for patients with renal dysfunction and a central line who have failed a labetalol drip. It is being recommended only for use in patients with a central line because the recommended concentration (ie, 0.1 mg/mL) provides too much fluid. More concentrated solutions of nicardipine cause phlebitis if given in a peripheral vein.

Invirase® is a hard-gelatin capsule form of the protease inhibitor saquinivir. Due to poor bioavailability, Fortovase®, a soft-gelatin capsule with better bioavailability, was marketed. In January of 2002, Invirase® was deleted from the *Formulary* because it was perceived that Fortovase® is a better product. Since this time, however, there are now new data that suggest that Invirase® is preferred when used in combination with ritonavir. Invirase® is given with ritonavir to improve the bioavailability of ritonavir.

Ritonavir increases the plasma concentrations of saquinavir by 2 mechanisms. It inhibits cytochrome P450 (CYP) in the gut during absorption and inhibits metabolic hepatic enzymes. The 20-fold increase in saquinavir plasma concentrations with concurrent ritonavir administration is most likely due to inhibition of cytochrome P450 enzymes at both sites. This results in marked increases in saquinavir peak serum concentrations.

Fortovase® has no effect on ritonavir pharmacokinetics. Therefore, the Anti-Infective Subcommittee recommended the re-addition of Invirase® in the *Formulary.*

Tizanidine is an oral alpha-blocker used as a skeletal muscle relaxant. It was reviewed by the P&T Committee in April 2002 and was not added in the *Formulary.* At that time, the P&T Committee determined that there was insufficient evidence to conclude that tizanidine was superior to baclofen or diazepam.

A recent evidence-based review of skeletal muscle relaxants included spasticity and musculoskeletal conditions. There are no published systematic reviews of the use of tizanidine for the treatment of musculoskeletal conditions.

3 comparative trials of tizanidine with other skeletal muscle relaxants in musculoskeletal conditions were located. 2 studies compared tizanidine with diazepam and 1 with chlorzoxazone (Parafon® Forte), which is not listed in the *Formulary.* All 3 studies concluded that tizanidine is equal to the alternative therapy.

1 study compared ibuprofen 400 mg (plus a placebo) with tizanidine plus ibuprofen. This study found physician-assessed "helpfulness" to be better in the combination group. The tizanidine group did have more central nervous system adverse effects (eg, sedation). Sedation is a common adverse effect of tizanidine.

There is no evidence that tizanidine (or any other skeletal muscle relaxant) is effective in the chronic management of musculoskeletal conditions (eg, low back pain).

When reviewed a year ago, tizanidine was about 30-times more expensive than baclofen. Tizanidine is now available as a generic from various manufacturers. Although the cost of tizanidine has decreased by about 50%, it is still many times more expensive than all of the other options.

Because tizanidine is as effective as the formulary alternatives (eg, cyclobenzaprine, ibuprofen), is listed in the Pain Committee's Adult Pain Algorithm, and should not significantly add to pharmaceutical expenditures, it was added in the *Formulary.* Although it is more expensive than other alternatives and is not a

(continued on next page)

OUTPATIENT PHARMACY

Surviving Florida Medicaid's Preferred Drug List

As a result of declining public resources, Florida Medicaid has undergone many changes in the past few years. All of these changes have resulted in a program that is much more restrictive for patients and providers. Further, Florida Medicaid is a notoriously poor communicator of their policy changes. Rejected online pharmacy claims remain the most common way pharmacists and prescribers find out about changes in Medicaid rules.

The biggest change Medicaid has made in recent years is the development of a formulary or list of preferred drugs. The list can be found on the Internet at http://www.fdhc.state.fl.us/Medicaid/Prescribed_Drug/pharm_thera/fmpdl.shtml. Patients covered by Medicaid are allowed 4 brand name drugs on this list and unlimited generic drugs. Brand-name drugs that do not count toward the 4-brand-name limit are antiretrovirals, oral contraceptives, mental health drugs (most medications for epilepsy as well), immunosuppressants, insulins, and glucose test strips. Pharmacists have found that some drugs not listed on the Preferred Drug List will be approved (eg, Oramorph® and MS Contin®); however, check with your pharmacist if you are unsure about whether a drug will be approved.

Permission to use non-preferred agents may be obtained by calling the Florida Medicaid processor at 1-877-553-7481. Pharmacists may call when patients exceed the 4-brand-name limit with preferred drugs. However, prescribers must call to request non-preferred agents.

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As a result of declining public resources, Florida Medicaid has undergone many changes in the past few years. All of these changes have resulted in a program that is much more restrictive for patients and providers.

A Medicaid pharmacist will ask specifics about the case and make a decision immediately. Patients typically receive their prescription within 4 hours. Thus, using therapeutically equivalent drugs on the Preferred Drug List can save time and trouble.

Medicaid also has a list of drugs that, although preferred agents, require prior authorization before they may be dispensed. This process requires that specific forms be filled out by the prescriber and submitted by fax. The forms require demographics and laboratory data necessary to justify the use of that drug in a particular patient.

Prior-authorization forms must also be submitted for pediatric patients. Pediatric patients who also have CMS coverage are not excluded from these requirements. Hospital policy requires that all other payers be billed before the CMS contract.

Generally, prescriptions processed at the pharmacy will be approved 24 to 48 hours after the submission of the requested information. Because many of these drugs are exceedingly expensive, drugs will not be dispensed to patients before being approved online by Medicaid. These rules leave many frustrated when patients are trying to be discharged, etc. *A list of the most commonly prescribed agents requiring prior authorization before any outpatient use is found in the table on the back page.*

Coordinators and physicians may save themselves frustration by keeping the various forms on hand and filing them prior to discharge. These forms are always kept in the Shands Outpatient and Medical Plaza Pharmacies. Pharmacy staff will be happy to assist you in this process.

by Bill Harbilas, PharmD

Formulary, *from page 2*
first-line agent, it does offer another therapeutic option in a different pharmacological class.

Candida skin test, mumps skin test, and **tetanus toxoid skin test** were all deleted from the *Formulary* because "controls" are no longer recommended for use with PPD skin testing. Mumps, tetanus (toxoid), and candida skins tests used to be routinely used as "controls" for anergy testing, which was thought to help interpret negative PPD skin tests.

The use of skin test controls used to be recommended by the Centers for Disease Control (CDC). The theory was that patients should react to at least 1 of these common antigens. If the PPD was negative, but all of the controls were negative, the negative PPD was considered to be indeterminate. Patients at risk of acquiring TB are also often immunocompromised (eg, patients infected with HIV).

Mumps skin test antigens are no longer marketed. Tetanus toxoid is in short supply. Candida skin test is not standardized and has questionable value. Therefore, the Anti-Infective Subcommittee recommended that these skin tests be deleted form the *Formulary* and be made nonformulary and not available.

Chloramphenicol ophthalmic solution has been removed from the market. The manufacturer removed it from the market because of decreased use and because of public and professional concerns about the risk of bone marrow aplasia (ie, aplastic anemia) with chloramphenicol.

There are alternatives that can be used to treat conjunctivitis, endophthalmitis, and ophthalmia neonatorum. Ofloxacin, ciprofloxacin, tobramycin, erythromycin, natamycin, Neosporin®, Polysporin®, bacitracin, and other compounded products can be used. Selection of an alternative is based on the type of infection and the known or suspected pathogen.

Inamrinone is a phosphodiesterase inhibitor with positive inotropic and vasodilatory activity. In July 2000, the generic name of amrinone was changed to inamrinone because of the continued confusion between amrinone and amiodarone. Inamrinone was deleted from the *Formulary* in June 2000. Milrinone is the phosphodiesterase inhibitor listed in the *Formulary*.

Inamrinone was listed as a high-priority drug because its use would be immediate — if prescribed. Therefore, the P&T Committee designated inamrinone nonformulary and not available. If a phosphodiesterase inhibitor is needed, milrinone will be recommended.

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POLICIES AND PROCEDURES

"Medically necessary" not necessary

In the outpatient setting, a prescriber can prevent generic substitution for a brand name product by writing "Medically Necessary" on the prescription. If "Medically Necessary" is not written, a less expensive generic will be dispensed.

In the inpatient setting, "Medically Necessary" does not have the same legal meaning when an order is written. If an order is written for a specific brand of a product with "Medically Necessary" included in the order, the generic product listed in the *Formulary* will still be dispensed. Drugs are listed in the *Formulary* as generics whenever possible. These products are equivalent to the brand name products and are AB-rated by the FDA.

If for any reason, an attending physician thinks that a specific brand must be used for a specific patient, please contact your decentralized pharmacist. For example, if a patient has an allergy to an inert ingredient in a specific product, special arrangement would have to be made for an alternative product. This would be acquired through the nonformulary process.

However, if an attending physician thinks that a specific brand should be used for all patients, this must be evaluated and approved by the P&T Committee. A specific brand will be listed in the *Formulary* only if there is scientific evidence to support the decision.

Attending physicians should send correspondence on this issues to the Secretary, Pharmacy and Therapeutics Committee, Box 100316, JHMHC.

Outpatient pharmacy, from page 3

DRUGS REQUIRING MEDICAID PRIOR-AUTHORIZATION

Generic Name	Brand Name
albumin	Various
aldesleukin (IL-2)	Proleukin®
alitretinoin	Panretin®
bexarotene	Targretin®
botulinium toxin type A	Botox®
botulinium toxin type B	Myobloc®
darbepoetin	Aranesp®
epoetin alpha (EPO)	Procrit®
filgrastim (G-CSF)	Neupogen®
food supplements	Various
human growth hormone*	Serostim®
immune globulin (IVIG)	Gamimmune®, others
iron glucose/sucrose	Venofer®/Ferrlecit®
modafanil	Provigil®
oxycodone SR	OxyContin®
pegfilgrastim (G-CSF)	Neulasta®
sargramostim (GM-CSF)	Leukine®
trimetrexate	Neutrexin®
valganciclovir	Valcyte®
voriconazole	Vfend®

* For HIV-wasting in adults