FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met August 19, 2008. Two drugs were added in the Formulary, 1 for a 4-month evaluation. 3 drugs were deleted, and 4 were designated nonformulary and not available. 2 interchanges were approved, and 1 drug was added to the Chemo-therapy Policy.

◆ ADDED

Desflurane (Suprane® by Baxter)*
  *Added for a 4-month evaluation

Fosaprepitant Injection (Emend® by Merck & Co)†
  †Restricted to clinical pharmacist approval (like aprepitant)

◆ DELETED

Cromolyn Inhalation Solution (Generics)‡
  ‡Nonformulary and not available

Phenytoin Injection (Generics) ‡§
  ‡§Nonformulary and not available; Interchanged to Fosphenytoin Injection

Stannous Fluoride Gel (Generic)‡
  ‡Nonformulary and not available

◆ NONFORMULARY AND NOT AVAILABLE

Glycerol, Sterile Anhydrous (Compounded)

◆ THERAPEUTIC INTERCHANGES

Ciprodex® (Ciprofloxacin + Dexamethasone) for Cipro® HC (Ciprofloxacin + Hydrocortisone)³
  ³4 drops Ciprodex® for 3 drops of Cipro® HC

Fosphenytoin (Generics) for Phenytoin Injection (Generics)”
  “Same dosage in phenytoin equivalents

◆ CRITERIA-FOR-USE CHANGES

Bendamustine (Treanda®)††
  ††Added in the Chemotherapy Policy

POLICIES AND PROCEDURES

New pediatric anticoagulation policies

At the June P&T Committee meeting, a new Anticoagulation Monitoring Policy was approved. This policy made several changes, which are required by the Joint Commission (TJC). All hospitals accredited by TJC must comply with the National Patient Safety Goals (NPSGs) for Anticoagulation (ie, Requirement 3E). This initiative is intended to reduce the likelihood of patient harm associated with the use of anticoagulation therapy, which has long been recognized as a high-risk medication. These requirements promote the use of standardized practices.

When the anticoagulation policy was approved in June, it did not include protocols for use in children. At the August P&T Committee, 2 policies were approved based on the patient’s age: Pediatric Heparin Protocol for Patients Less than 12 Years of Age and Pediatric Heparin Protocol for Patients Older Than 12 and Less than 18 Years of Age. These protocols are limited to the Pediatric Intensive Care Unit (PICU) or Intermediate Care Units (IMCs). Heparin will be provided only in a standard concentration (ie, 100 units/mL), with the size of the bag determined by the patient’s age (ie, 50 mL or 250 mL). There is a standard loading dose (ie, 80 units/kg) and standard starting dosage (ie, 18 units/kg/hr).

Standard monitoring includes the use of unfractionated heparin levels with adjustments to the dosage based on the measurements. The target heparin level is 0.3 to 0.7 units/mL. Additional monitoring is specified (eg, daily CBC and platelet count) with guidelines for notification of the prescribing physician (eg, when bleeding occurs or platelet counts drop).

The approval of the pediatric heparin protocols maintains our efforts to be ahead of TJC’s 2008 National Patient Safety Goals for Anticoagulation.

Therapeutic interchange – 2008

A drug is ordered, but a different drug is dispensed and administered. The drug that is dispensed is not a generic equivalent of the ordered drug, but it is a “therapeutically equivalent” product. A single drug product is selected and listed in the Formulary for a therapeutic class. The drugs are not the same, but they are so similar that there is no clinically significant difference among the drugs in a class. All non-selected drugs are changed to the formulary class representative. The non-selected drugs are nonformulary and are not available—with a few exceptions.

This is therapeutic interchange. Therapeutic interchange is the substitution of various therapeutically equivalent drug products by pharmacists under arrangements of the authorized prescribers who have agreed on the conditions for the change.

Therapeutic interchange is reviewed and approved by the medical staff by the Pharmacy & Therapeutics (P&T) Committee, which is a medical staff committee. Representatives from various medical specialties participate in the P&T Committee. If a drug class is used by a specific medical specialty and a representative from that medical specialty is not on the P&T Committee, the department head is contacted to

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INSIDE THIS ISSUE

◆ Insulin pen stability

(continued on next page)
desflurane was added in the Formulary and restricted to approval by an oncology pharmacist in August 2003. Like aprepitant, fosaprepitant was added in the Formulary and restricted to approval by an oncology pharmacist.

**Cromolyn** is a mast cell stabilizer. The solution for inhalation was used as a prophylactic agent for the prevention of mild to moderate asthma. The use of cromolyn by oral inhalation has been very limited due to the availability of superior agents. King Pharmaceuticals discontinued the manufacture of Intal® (cromolyn solution for nebulization), and there is no other manufacturer of this product. The product has not been recalled from the market, and it may take several months before supplies stocked in community pharmacies are exhausted or go out of date.

According to the letter from King Pharmaceuticals, the decision to discontinue this product was “based upon many factors, including [their] understanding of current medical therapy, and the availability of alternative asthma therapies.” Therefore, effective immediately, cromolyn sodium solution for inhalation and drops for nasal spray (Nasalcrom®) are no longer available. Cromolyn nasal spray (Nasalcrom®) remains listed in the Formulary.

**Intravenous phenytoin** was designated nonformulary and not available and will be interchanged to an equivalent dosage of fosphenytoin in phenytoin equivalents. The implementation date for this interchange will be October 1st.

The decision to eliminate the use of IV phenytoin came after the restrictions were lifted from fosphenytoin injection at the June P&T Committee meeting. The Department of Pediatrics expressed their support for an automatic interchange to fosphenytoin for children. Rather than have separate systems for adults and children, the proposal was evaluated for all patients.

An article was published in the July-August issue of the Drugs & Therapy Bulletin announcing the proposal to delete phenytoin injection from the Formulary. Only 1 comment was received, and it was supportive of the deletion and interchange.

**Stannous fluoride** is a topical agent used for the prevention of dental caries or for dental desensitization. This product has not been used at Shands at UF, Shands Vista, or Shands Rehab Hospital. Because of lack of use, stannous fluoride gel was deleted from the Formulary and designated nonformulary and not available.

**Sterile anhydrous glycerol** was originally evaluated by the P&T Committee in April 2005 for possible addition in the Formulary. It was requested for use by radiologists for chemical rhizotomies, which are nerve ablations used in the treatment of trigeminal neuralgia.

Since there is no commercially available product, sterile anhydrous glycerol would have to be obtained from an outside compounding pharmacy that compounds sterile products from non-sterile ingredients. It can be obtained only on a patient-specific basis and cannot be added in the Formulary. In order for sterile anhydrous glycerol to be used formulary, a patient would have to give informed consent. This informed consent document has not been developed; therefore, sterile anhydrous glycerol was designated nonformulary and not available.

In January 2005, CiproDex® was added in the Formulary and Cipro HC® was deleted and designated nonformulary and not available. CiproDex® has a labeled indication for otitis media with tympanostomy tubes and otitis externa. Otic fluoroquinolone suspensions are used for various off-labeled otic infections for which there is little scientific evidence of efficacy. However, the otitis media data are considered applicable for other otic infections.

Evidence shows that ciprofloxacin combined with a topical steroid significantly increases clinical cure rates when compared with monotherapy for the treatment of acute otitis media with otitis externa. Topical steroids are added to fluoroquinolones to reduce inflammation and enhance clinical response rates.

An additional benefit for CiproDex® is that it is a sterile product. Cipro HC® is not sterile. Despite this information, Cipro HC® continues to be ordered even though it is not available. Therefore, CiproDex® will now be automatically interchanged for Cipro HC® using 4 drops of CiproDex® for 3 drops of Cipro HC®.

**Bendamustine** is an oral cytotoxic drug with alkylating agent and purine analogue actions. It has a labeled indication for the treatment of chronic lymphocytic leukemia (CLL). It may have off-labeled uses for non-Hodgkin’s lymphoma, multiple myeloma, breast cancer, or other cancers. Bendamustine was not added in the Formulary, but it was added to the Chemotherapy Policy. If requested for nonformulary use, bendamustine must be ordered on a Chemotherapy Order Form.
Why are insulin pens “less stable” than insulin vials?

Many hospitals have switched from using vials to using pens for various insulin products. Insulin pens have several advantages, including clear labeling on each pen (instead of using unlabeled syringes and a vial). The pens are in a ready-to-use form and require less nursing time to prepare. Pens are also a dosage form that allows diabetes educators to teach patients recently diagnosed with diabetes how to administer the insulin that they will use once they are discharged from the hospital. However, a disadvantage of insulin pens is the shorter stability of these products when they are “in use” and kept out of the refrigerator. This can lead to product waste. Unopened insulin vials and pens are stable until the expiration date on the vial or pen when stored in the refrigerator. A refrigerator maintains temperatures of 2°C and 8°C (36°F and 46°F). Once a vial or pen is “in use,” it is no longer necessary to store the product in the refrigerator. The maximum time that multi-use vials (or pens) can be stored is 28 days according to product labeling and USP guidelines. This, of course, presumes that the vial will be stored at room temperature and that excursions from this temperature will not occur. Room temperature is thermostatically maintained between 20°C to 25°C (ie, 68°F to 77°F). Room temperature guidelines do allow brief exposures to temperatures as high as 40°C (ie, 104°F). The extreme heat of Florida or the freezing cold temperatures that many of us fled to Florida in order to avoid can affect the stability of insulin products that are “in use.”

When stored at room temperature, insulin vials have “in-use” stabilities of 28 days, while pens are stable only for 7 to 14 days (ie, depending on the individual product’s labeling). Therefore, insulin pens must be discarded after 10 days at Shands at UF (based on the shortest labeled stabilities of the pens that we stock). This has caused some to question why the insulin in pens is less stable than when it is stored in a vial. It turns out that this is a fairly difficult question to answer.2,5

The shorter stabilities of insulin pens come from guidelines recommended by the FDA for insulin pens and cartridges. The recommendations in the guidelines for pens and cartridges differ from those for vials based on differences in the expected usage patterns for these products.

The shorter stabilities of insulin pens come from guidelines recommended by the FDA for insulin pens and cartridges. The recommendations in the guidelines for pens and cartridges differ from those for vials based on differences in the expected usage patterns for these products. According to pen manufacturers, stability guidelines established by the FDA for pens and cartridges consider 2 factors.2,4 The first factor is the smaller volume and fewer total units of insulin supplied in the pen cartridge compared to a vial. The smaller volume is expected to lead to a more rapid exhaustion of the insulin in the cartridge compared to the vial. The other factor is the increased convenience of the pen. The increased convenience of the pen is expected to result in patients exposing their insulin to thermal and agitation conditions that would be greater than the exposure for insulin in vials.

The testing conditions used for determining the in-use dating for the cartridges are consistent with an expected increase in the thermal and agitation exposure of insulin in cartridges compared to insulin in vials. Thus, the testing conditions for vials and cartridges differ, which leads to different storage guidelines for vials and pens.

The current in-use storage recommendations for insulin pens are based on exposure to conditions that are severe and are not truly reflected by room temperature storage in the hospital setting. It is likely that insulin pens are stable for more than our current practice of dating pens and only using them for at most 10 days in the hospital setting. Official labeling of insulin pens in Europe have in-use stabilities of 21 to 28 days.5 The current FDA standards are more stringent than those used in other countries.

Since most patients are hospitalized for less than 10 days, the waste of insulin often occurs when the patient is discharged and not based on short stability. Insulin pens dispensed to inpatients are not labeled for outpatient use and cannot be sent home with the patient.

Although it is unlikely that the true stability of insulin pens is only 10 days, there is no published evidence that allows use beyond the current official labeling of these products. Therefore, insulin pens must be dated when they are put in use and discarded after 10 days.

REFERENCES
1. Anonymous—Probable, possible, or definite
And we’ll do the rest!

To Report an Adverse Drug Reaction

Call the ADR Hotline: 5-ADRS (5-2377)

PROVIDE:
- Patient’s name
- Patient’s location
- Suspected drug(s)
- Type of reaction
- Whether the reaction was probable, possible, or definite
- Your name and pager # or extension

ADR HOTLINE: 5-ADRS
Therapeutic interchange, from page 1

solicit input on that particular inter
change.

Therapeutic interchange has been prac
ticed for over 20 years at Shands at UF. Feedback from both attendings
and housestaff consistently support the
concept of interchanging to a product
that is currently available, rather than
constantly paging to have a new order
written. Some institutions list only 1
agent in the class and constantly con
tact the prescriber to change the order
to the formulary agent.

Since the medical staff are not con
tacted to write a new order, there has
to be a mechanism to notify the medical
staff and nursing when an interchange
occurs. When a drug is prescribed that
is interchanged, documentation of the
interchange is placed in the chart. This
documentation is placed in both the
Physicians Orders section of the chart
and the Progress Notes section. The
notation in the Orders section notifies
the patient’s nurse of the change. The
note in the Progress Notes notifies the
medical staff.

There can be exceptions made to
the interchange policy. If the patient
has a rational reason not to receive
the interchanged drug (ie, allergic to a
dye in the interchanged product), the
change can be overruled. Experience
has shown that these situations are
very rare.

A continually updated version of the
drugs that are therapeutically inter
changed can be found after logging
on to the Shands Portal at https://
my.portal.shands.ufl.edu/portal/page/
portal/DEPT_CONTENT/Pharmacy/UF/
Formulary/TherapeuticInterchange.

Often when a new product is added to
the list, prescribers are notified that be
ginning the next month an interchange
will occur. This gives prescribers an
opportunity to change their habits.

Most prescribers use the preferred
agents. Interchanges are relatively
infrequent—once the housestaff and
other prescribers know the drug that is
listed as the “class representative.”

Combination products also will be
interchanged when the ingredients are
listed in the Formulary and the exact
amount of each ingredient is available.

For example, an order for Vytorin®
10/10 will be changed to Ezetimibe 10
mg [Zetia®] and Simvastatin [Zocor®] 10
mg. The same documentation as for the
therapeutic interchanges will occur.

There is concern that patients get
ning switched to a different drug during
their hospitalization will be discharged
on the new drug, then resume their old
medication, resulting in therapeutic du
plication and possible adverse effects.

Prescribers must take this into consid
eration during the medication reconcili
ation process. When an interchange
occurs, it is noted on the Transfer
Medication Report and the medication
administration record (MAR). Often,
it is best to switch patients back to
the medication they were admitted on,
which may be preferred by the
patient’s third-party payer. The Home
Medication Profile should always be
reviewed when discharge medications
are prescribed.