

Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met February 16, 2010. 1 drug was added in the *Formulary*, and 3 products were deleted. 5 products were designated nonformulary and not available with 3 interchanges approved.

◆ ADDED

Pantoprazole IV
(Protonix® IV by Wyeth)*

*Restricted to patients on clopidogrel

◆ DELETED

Ascorbic Acid Drops (Cecon®)†
†Nonformulary and not available

Ropivacaine 0.3% in Normal Saline (Compounded)‡
‡No longer available pre-mixed

Triamcinolone MDI (Azmacort®)†
†Nonformulary and not available

◆ NONFORMULARY AND NOT AVAILABLE

Olanzapine ER Injection
(Zyprexa® Relprevv®)§
§NFNA at Shands at UF only

Phenol, Sterile Injection
(Compounded)

Torsemide
(Demadex® and Generics)

◆ INTERCHANGES

Brimonidine Opth 0.2% for Alphagan® P 0.15%

Bumetanide for Torsemide¶
¶Approximately 0.5 mg bumetanide for each 5 mg torsemide

Risperidone ODT for Risperidone Liquid**

**Switched only at Shands Vista

(continued on next page)

POLICIES AND PROCEDURES

Cracking down on outpatient controlled substances

Drug diversion is a problem faced by healthcare practitioners seeking a balance between pain control and over-prescribing. Diversion can be identified through careful observation of prescription refill patterns, patient filling behavior, and the filling of multiple scheduled or as-needed opioid pain relievers. Shands Outpatient Pharmacy has recently revised its policy regarding all controlled drugs — including opioids, steroids, and amphetamines

◆

Newly revised Shands policies and new Florida laws enable providers to monitor controlled-substance use more closely. Diversion should decrease with closer attention to early refills and signs of diversion, and by instituting quantity maximums on outpatient prescriptions.

— to control inventory, decrease the likelihood of theft, and prevent diversion. These policies have been approved by the Clinic Safety Committee and endorsed by the Pharmacy and Therapeutics Committee to maintain consistency between prescriptions written for discharge and outpatient pharmacy policies.

To prevent diversion, the new policies include restrictions on early prescription refills and quantities allowed. An early refill is defined as a prescription that is requested when there should still be at least 10% of the prescription remaining. This will

be evaluated by calculating the days' supply using the maximum dose and assessing when less than 10% of the prescription should be remaining. Prescriptions will be available only after that date. Exceptions to this policy will be handled on a case-by-case basis through the pharmacy manager, clinical pharmacist, dispensing pharmacist, and physician, when necessary.

Controlled substances will also now be restricted to a maximum of 500 tablets-per-prescription. Prescriptions with quantities greater than this amount will be reduced to 500 or dispensed as a 2-week supply with prescriber notification. Drugs that will most commonly be affected by this new quantity restriction are morphine, hydromorphone, oxycodone, and methadone. The outpatient pharmacy will attempt to keep a minimum of 2000 tablets of the commonly prescribed controlled substances but must maintain a balance with inventory control. Controlled substances available through the outpatient pharmacies will also be limited through the formulary process. According to current Drug Enforcement Agency (DEA) restrictions, prescriptions cannot be post-dated but may be written for future filling by clearly indicating on the prescription a "do not dispense before <insert date>." Prescriptions may be filled on or after the specified date, but not before. Each filled prescription may be for up to a 30-day supply and the total amount of future filling cannot exceed a 90-day limit.¹

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INSIDE THIS ISSUE

- ◆ Indications and the *Formulary*
- ◆ "Smart Pump Guardrails"
- ◆ PCA order forms

Formulary update, from page 1

Pantoprazole is a proton-pump inhibitor (PPI) that is available as oral and intravenous dosage forms. There are 6 oral PPIs, but only 2 injectable PPIs (esomeprazole and pantoprazole). With the addition of pantoprazole in the *Formulary*, both injectable PPIs are now available. IV pantoprazole is restricted to patients on clopidogrel [Plavix®] with a gastrointestinal (GI) bleed who will be undergoing a therapeutic endoscopy. An active GI bleed requires a constant infusion of a PPI, otherwise an oral PPI (lansoprazole) is preferred.

The addition of IV pantoprazole in the *Formulary* was in response to ongoing concerns about interactions between clopidogrel and PPIs. There is conflicting information about the significance of these interactions or whether there are differences among the PPIs; however, current labeling for omeprazole and esomeprazole states that these agents should be avoided in patients receiving clopidogrel. Clopidogrel is a prodrug and must be converted by CYP2C19 to its active metabolite. Omeprazole and esomeprazole inhibit CYP2C19, which could decrease clopidogrel's effectiveness. Oral lansoprazole can be used when patients do not have an active GI bleed.

Ascorbic acid drops were deleted from the *Formulary* and designated nonformulary and not available because they are no longer available from their manufacturer. There are no alternative suppliers for this product.

Ropivacaine in normal saline is a pre-mixed bag of a long-acting amide local anesthetic that is used for epidural pain control. The pre-mixed bags containing 0.3% ropivacaine in 250 mL normal saline were discontinued due to lack of use. These pre-mixed bags were being purchased and used to stock automatic dispensing cabinets; however, increased wastage led to the discontinuation of this dosage form. This concentration of ropivacaine will now be compounded on an as-needed basis.

Triamcinolone metered-dose inhalers were discontinued by its manufacturer. There is no other supplier for this product. Therefore, this dosage form was deleted from the *Formulary* and designated nonformulary and not available.

Triamcinolone was originally added in the *Formulary* in 1990 because of its potency, patient acceptance, and reasonable cost. Fluticasone MDIs remain listed in the *Formulary*.

Zyprexa® Relprevv® is a long-acting intramuscular dosage form of olanzapine, which is given every 2 to 4 weeks.

Olanzapine is an atypical antipsychotic drug most commonly associated with weight gain and the risk of the development of diabetes. For this reason, its use has been declining.

The P&T Committee determined that there should be no need for this agent in the inpatient setting at Shands at UF. Shands Vista has other long-acting injectable antipsychotics. Therefore, Zyprexa® Relprevv® was designated nonformulary and not available at Shands at UF.

Sterile phenol injection has been used for nerve ablations at other institutions. Since it is a sterile product compounded from nonsterile ingredients, it cannot be made at Shands at UF. It must be obtained on a patient-specific basis and cannot be listed in the *Formulary*.

Since sterile phenol is made from nonsterile ingredients, an informed consent must be approved by the Legal Department and the P&T Committee must review the product and determine that the potential benefits outweigh any risks. If the evidence is sufficient, sterile phenol could be designated a high-priority, nonformulary drug with computer entries explaining the method of obtaining product.

There are limited data to support the use of sterile phenol and sufficient evidence has not been submitted to the P&T Committee for review. Thus, it was deemed nonformulary and not available by policy.

Torsemide is a loop diuretic approved by the FDA in 1993. Torsemide was considered for addition in the *Formulary* because of persistent nonformulary use.

Torsemide is available as an oral formulation with labeled indications including edema, congestive heart failure (CHF), ascites, and hypertension. Torsemide is not unique in the loop diuretic class. Shands currently has furosemide (Lasix®), bumetanide (Bumex®), and ethacrynic acid (Edecrin®) listed in the *Formulary*. Torsemide's claimed advantages over furosemide include a 24-hour dosing interval, a more predictable bioavailability even in patients with decompensated heart failure, less renal excretion of calcium, potassium, and magnesium, and a more pronounced diuresis than other drugs in its class.

Torsemide undergoes rapid absorption with a bioavailability of around 80%. Comparatively, furosemide's bioavailability is more variable (ranging from 11–90%), while bumetanide's is similar to torsemide's. The variability of furosemide's bioavailability makes interchange of furosemide to other diuretics difficult, especially in patients with decompensated heart failure.

Studies show that torsemide has a unique pharmacologic property in the loop diuretic class; it has demonstrated mild inhibition of the renin-angiotensin-aldosterone system (RAAS), a property that may have additive beneficial effects in patients with CHF. Similar to spironolactone, torsemide has shown a reduction in mortality compared to other diuretics in HF, although this was just 1 clinical trial with multiple obvious limitations.

In outpatient settings, torsemide, compared to furosemide, has demonstrated a lower rate of first hospitalization for CHF, re-hospitalizations, and hospitalizations for any cardiac cause in multiple trials. This was subsequently shown in pharmacoeconomic studies to have a reduced overall treatment cost from a health-care system perspective, although the acquisition cost of torsemide is higher than either furosemide or bumetanide. In addition, the cost of storage and distribution of a drug used so infrequently at Shands is significant. Also, pharmacokinetic and dynamic properties of torsemide are very similar to bumetanide, albeit without the added benefit of mild RAAS inhibition. Also, an exhaustive search of the literature has revealed no appreciable measurable difference in patients experiencing brief, acute inpatient changes in their loop diuretic medication from one to another, aside from diuretic resistance, which is possible with any drug in this class.

Torsemide was designated nonformulary and not available with a therapeutic interchange to bumetanide in the inpatient setting. The following interchanges will be made: convert torsemide 5 mg to bumetanide 0.5 mg; convert torsemide 10 mg use bumetanide 1 mg; convert torsemide 20–60 mg to bumetanide 2 mg; convert torsemide 61–80 mg to bumetanide 3 mg; and, convert torsemide 100 mg to bumetanide 4 mg.

Brimonidine is an alpha-agonist used for the treatment of glaucoma. **Alphagan-P®** 0.15% has been listed in the *Formulary*. Generic brimonidine 0.2% costs about 20-times less than Alphagan-P®. Therefore, a drop for drop interchange was approved.

Risperidone is an atypical antipsychotic agent. The oral liquid and **orally disintegrating tablet (ODT)** are often used as an alternative to an injection when patients need treatment for agitation. The ODT dosage form is more convenient to use for some patients. For this reason, there will be an automatic interchange from risperidone liquid to an equivalent ODT dose at Shands Vista.

POLICIES AND PROCEDURES

Approved criteria for use

The Joint Commission requires a diagnosis, condition, or indication for use for each drug ordered. This information can be anywhere in the medical record (eg, medical history) and need not be on the order itself. Whether each diagnosis, condition, or indication has been considered by the P&T Committee determines a drug's formulary status. For example, a drug listed in the *Formulary* but being used for an indication not approved by the P&T Committee would be considered a nonformulary use. There needs to be procedure for "nonformulary" uses of drugs.

The P&T Committee always evaluates reasonable uses for drugs when it is added in the *Formulary*. When necessary, restrictions to specific indications may occur (eg, restricting the use of antibiotics to prevent resistance). However, all drugs listed in the *Formulary* do not currently have these criteria.

Therefore, by policy, all drugs listed in the *Formulary* are approved for all labeled indications and off-labeled uses listed in DrugDex®, unless the P&T Committee approves more restrictive criteria for use. DrugDex® is the primary drug reference available on the Shands HealthCare Portal.

POLICIES AND PROCEDURES

Alaris® pump guardrails

You order an IV drug to be administered at 1 mcg/kg/hr. The correct IV drug in the right concentration of fluid is delivered to a nurse but an extra zero is inadvertently hit while entering the rate (ie, 10 mcg/kg/hr) into the IV infusion pump. If that dose is administered, there is potential for significant patient harm. Thankfully, the "smart" pump sounds an alarm and the mistake is caught; the correct dose is programmed into the pump. A significant error has been averted.

Recently Shands and UF have made a major investment in Alaris® "smart" IV infusion pumps that decrease over- and under-doses of critical drugs. These pumps are "smart" because they are programmed with the drug, concentrations, and acceptable dosage limits. The amount of drug being delivered is calculated by the pump, and when the dosage is outside of acceptable limits, an alert fires.

There are 2 types of limits: "soft" limits and "hard" limits. Soft limits are informational but give the nurse the opportunity to override the alert. Hard limits prevent the drug from being administered without a change in the dosage, concentration, and/or duration.

The most difficult part about implementing "smart" pumps is creating the knowledge base or "library" of acceptable dosages that will result in alerts. Unlike many technologies, smart pumps do not come with pre-loaded dosage ranges. This has its advantages and disadvantages.

Often technologies with pre-loaded drug dosage limits are too conservative. This leads to too many alerts.

Alert fatigue contributes to these alerts being ignored, which decreases the safety impact of the technology. Commercial knowledge base vendors are too conservative, presumably because they fear liability if the limits are too liberal.

Creating a dosage-limits library for the Alaris® pumps was a massive undertaking at Shands at UF. It took input and collaboration from nursing staff, pharmacy staff, and physicians throughout the institution. It required the standardization of IV concentrations. It takes continuous monitoring of the alerts generated and adjustments to these limits so they prevent dosage errors but do not alert when the dose is reasonable.

The P&T Committee reviews and endorses the process by which the Alaris® pump library is established. When there is disagreement about the appropriate dosage limits, the P&T is the final judge on what limits should be set. The Alaris® pump library is available on the Portal.* If an attending physician would like to have these limits modified, please contact the Alaris Team at Alaris@shands.ufl.edu. Disputes between the Alaris Team and the requesting physician will be resolved by the P&T Committee, if necessary.

LINKS

*https://my.portal.shands.ufl.edu/portal/page/portal/DEPT_CONTENT/Pharmacy/UF/Drug-Info/Smart-Pumps/Alaris_Pump_Guardrails_%20Library.pdf

PRESCRIBING

Adult PCA order form

Since September 2009, a mandatory *Pediatric PCA Order Form** has been required if patient-controlled analgesia is used on any pediatric patient. The purpose of the mandatory form is to promote the safe and effective use of patient-controlled analgesia in children. The *Pediatric PCA Order Form* was developed by the Department of Pediatrics and made mandatory by the P&T Committee at their request.

This concept was evaluated for possible extension to adults (ie, a mandatory order form for adults). After much consideration, the P&T Committee did not make the *Adult Patient-Controlled Analgesia Orders* form† mandatory. It is, however, listed on the Portal for use in patients who have not developed tolerance to opioids. The *Adult Patient Controlled Analgesia Orders* form is recommended for opioid-naïve patients and should promote safe and appropriate use of patient-controlled analgesia in these adults.

The decision not to make the *Adult PCA Order Form* mandatory was based on the difficulty in handling opioid-tolerant patients who require concentrated opioid solutions. Trying to address these patients on a 1-page form with standardized concentrations was complicated. Good mandatory forms should be simple to use while promoting consistent, best practices.

The *Adult Patient-Controlled Analgesia Orders* form lists options for morphine, hydromorphone, and fentanyl PCA. It provides recommendations for loading doses, PCA doses, lockout intervals, 1-hour limits, and basal rates. Dosages are provided for supplementation for breakthrough pain. Patient-monitoring orders are included with instructions on when to stop the PCA and administer naloxone if the patient's respiratory rate decreases. Promethazine orders for nausea and nalbuphine for pruritus are listed, but these are optional.

LINKS

*https://my.portal.shands.ufl.edu/portal/page/portal/DEPT_CONTENT/Forms/UF/Tab6/81212.pdf

†https://my.portal.shands.ufl.edu/portal/page/portal/DEPT_CONTENT/Forms/UF/Tab18/67795.pdf

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Policies and procedures, from page 1

In addition to the restrictions on early refills and excessive quantities, the policy addresses diversion through prescription selection. When a patient presents a prescription for both a controlled and a non-controlled substance, if the patient selects to fill only the controlled substance, the prescriber will be notified. The prescriber will then dictate whether it is appropriate for the patient to receive only the controlled substance. This will help alert the provider to potential diversion. Potential diversion of any controlled substance will be investigated and documented in the patient's pharmacy record.

Patients should receive no more than one opioid for breakthrough pain in addition to one scheduled opioid. If a patient is found to have been prescribed more than this, the provider will be contacted to clarify the intended products; however, exceptions may be made on a case-by-case basis. When a provider is transitioning a patient from one opioid to another, it should be indicated on the prescription so that the pharmacist may check the new prescription for the proper opioid dose conversion. This transition between opioids may involve a patient having two scheduled or breakthrough opioid prescriptions but is allowed without

provider contact as long as it is indicated on the prescription that a transition is occurring. Opioid conversion should be in a manner consistent with current guidelines and unreasonable conversions will be clarified with the provider. Guidelines for non-cancer pain can be found at [http://www.jpain.org/article/S1526-5900\(08\)00831-6/abstract](http://www.jpain.org/article/S1526-5900(08)00831-6/abstract), whereas guidelines for cancer pain and methadone switching can be found at <http://www.supportiveoncology.net/journal/articles/0101052.pdf>. According to the guidelines, when converting to methadone for non-cancer pain, a maximum dose of 30 mg q3h PRN should be utilized until after day 5 when a total daily dose can be calculated. This is due to the increased risk of respiratory depression due to methadone's long and variable half-life that complicates calculating an equianalgesic dose.²

New state laws will also be enacted by the end of 2010 to prevent controlled-substance diversion. Currently, a person is required to present a photo ID when picking up or receiving a prescription. Mail order prescriptions require a signature and courier identification. Physicians may also request that only the patient pick up a controlled prescription, which should be indicated on the first prescription. In addition, a Florida law that goes into effect

December 1, 2010, mandates a tracking process for controlled-substance dispensing. Each time a controlled substance is filled, a report will be sent by the dispenser to the Department of Health and entered into a database. A pharmacy, prescriber, or dispenser may then request patient specific reports from the database to monitor controlled prescription use. Data collected will include provider, pharmacy, and patient information, in addition to the date filled, method of payment, and name, strength, and quantity of the controlled substance.³

These newly revised Shands policies and new Florida laws enable providers to monitor controlled-substance use more closely. Diversion should decrease with closer attention to early refills and signs of diversion, and by instituting quantity maximums on outpatient prescriptions.

by Robyn Keen, PharmD

REFERENCES

1. Code of Federal Regulations Chapter 11 section 1306.12 accessed online at http://www.access.gpo.gov/nara/cfr/waisidx_09/21cfr1306_09.html
2. American Pain Society–American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain* 2009;10: 113-30
3. Florida Statutes Section 893.055 accessed online at <http://leg.state.fl.us/STATUTES>