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Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met May 20, 2003. 2 drugs or dosage forms were added in the *Formulary*. 1 drug was deleted and several products were designated not available.

◆ ADDED

Pancrelipase
(Ultrase® MT 20 by Axscan)*

**interchanged for Creon® 20 and Pancrease® MT 20*

Succimer
(Chemet® by Sanofi-Synthelabo)

◆ DELETED

Triazolam
(eg, Halcion® by Pharmacia & Upjohn)

◆ NONFORMULARY AND NOT AVAILABLE

Morphine, Extended-Release**
(eg, Avinza®, Kadian®***, MS Contin®)

***Oramorph® is the only extended-release morphine in the Formulary.*

****Kadian® is available only at Shands Rehab Hospital*

Pancrelipase products were reviewed to standardize what is listed in the *Formulary* in February. The Ultrase® MT product line was selected as the only pancrelipase brands that will be available. Ultrase® is less expensive than Creon® or Pancrease®, which were the other brands considered.

Ultrase® MT-20 has been added to substitute for Creon® 20 and Pancrease® MT-20. Originally Ultrase® MT-18 was used for this interchange. Now, Ultrase® MT-18 is substituted only for Pancrease®

(continued on next page)

DRUG INFORMATION FORUM

Micromedex now available

Clinical Pharmacology is the primary electronic drug information database available at Shands at UF. It has many useful features, including concise drug monographs and drug interaction reporting. Clinical Pharmacology is available to the medical staff and Shands at UF staff at http://cpip.gsm.com.

Recently, 4 new drug information databases, which are part of the MICROMEDEX® Healthcare Series, have been made widely available through the Health Center Library's website. *DRUGDEX®*, *POISINDEX®*, *IDENTIDEX®*, and *Martindale's Extra Pharmacopoeia* are now available. Any terminal with a ufl.edu IP address can access these databases. This includes any university-based computer, computers in all clinics, and all Shands at UF computers. Affiliated hospitals (eg, Shands at AGH) do not have access.

The MICROMEDEX® Healthcare Series databases will be listed in the Health Science Center Library website at http://www.library.health.ufl.edu under the database page. *DRUGDEX®*, *POISINDEX®*, *IDENTIDEX®*, and *Martindale* are also listed as access points with links to the MICROMEDEX® Healthcare Series.

DRUGDEX® is a general drug information reference. It is comprehensive and has information on less common adverse effects and off-label uses not found in *Clinical Pharmacology*. It is extensively referenced.

POISINDEX® is the gold-standard electronic reference for information on clinical toxicology. If a patient presents with an acute overdose, *POISINDEX®* is the primary reference used by regional poison control centers. It provides information on the toxic effects of drugs and other substances and how to manage toxic exposures.

IDENTIDEX® is a subsection of the *POISINDEX®* system, which can be accesses using the Toxicology link. This reference can be used to identify an oral solid dosage form based on its unique imprint code. Prescription and over-the-counter (OTC) drugs must have a unique imprint according to federal law. This imprint can be used to identify the tablet or capsule. Unfortunately, there is no federally funded or federally maintained list of these imprint codes. Commercial references must be used to match an imprint code with a drug's identity.

Clinical Pharmacology will also identify capsules and tablets. This function can be found under the Drug Products tab using the Product Identification link. Our own research has found that *IDENTIDEX®* is better at identifying imprint codes, especially for OTC products.

Martindale is a British reference produced by the Royal Pharmaceutical Society. It provides useful information about foreign drugs. Foreign brand names can be identified. There is also useful information about off-label uses and adverse drug effects.

MICROMEDEX® also allows free access for UF and Shands faculty, staff, and students to download their PDA-based drug reference *mobileMICROMEDEX®*. This database will work with both Palm OS® and Pocket-PC based PDAs.

If you have any questions or comments about this new database, please send an e-mail to hatton@ufl.edu.

INSIDE THIS ISSUE

◆ Drug shortages

◆ Beta-blockers and asthma

◆ Patients' own meds

Formulary update, *from page 1*
MT-16. Ultrase® MT-12 is interchanged for Pancrease® MT-10 or Creon® 10. When these interchanges are done, they will be documented as a "P&T Committee-Authorized Interchange" in the patient's chart.

Succimer is a chelating agent recommended for the treatment of lead and other heavy-metal toxicities. Although never listed in the *Formulary*, the Pharmacy has long kept a small supply of succimer available for the treatment of patients with lead toxicity. Succimer was added to the high-priority nonformulary drug list when it was recently ordered through the nonformulary process.

Changes in the nonformulary process mandate that nonformulary drugs be categorized as high, medium, or low priority. High-priority drugs will be evaluated as soon as possible to determine whether they should be listed in the *Formulary*. A high-priority drug is one that could result in significant patient harm if there is a delay in acquiring the drug product.

Other chelating agents used in the treatment of lead poisoning (ie, calcium disodium edetate [EDTA], dimercaprol [BAL], and penicillamine) and the treatment of other heavy-metal poisonings (deferoxamine) are already listed in the *Formulary*. Although rarely used, standard antidotes for heavy-metal poisonings are listed in the *Formulary* so they are available when they are needed.

Limited data exist regarding succimer's efficacy in improving symptoms related to lead encephalopathy. Data show that succimer effectively removes lead from patients with lead poisoning. However, there are limited data that correlate the lowering of lead levels with improvements in patients' outcomes. Standard references (eg, Poisindex) list succimer as a first-line agent for the treatment of lead toxicity.

Patients with moderately elevated blood lead concentrations (ie, 20 to 44 mcg/dL) have not shown improvements in outcomes when treated with succimer. Despite rapidly lowering blood lead concentrations, there were no discernible improvements in cognitive function compared with placebo.

Triazolam is a short-acting benzodiazepine hypnotic. It has been listed in the *Formulary* for many years. After temazepam was added in the *Formu-lary* in March, it was noted that tri-azolam is rarely used. Since triazolam is rarely used, it was deleted from the *Formulary*.

Oramorph® is the **extended-release morphine** listed in the *Formulary*. All other extended-release morphine products are nonformulary and not available.

Oramorph® has been the only extended-release product listed in the *Formulary* since 1996. At that time, only 2 extended-release morphine products were available: Oramorph® and MS Contin®. These products should be given twice a day.

Once-daily extended-release morphine products like **Avinza®** and **Kadian®** are not available at Shands at UF. These products are 1.5 to 2 times more expensive than Oramorph®. Also, there is limited space available for storing controlled substances (ie, in the SureMed® cabinets). Kadian® will be available only at the Shands Rehab Hospital.

SHORTAGES

Want more information about drug shortages?

More than ever, there is a critical shortage of drugs. Prescribers are justifiably frustrated. Pharmacists often receive questions about why these shortages are occurring and what can be done when they do occur.

A drug shortage can be caused by changes in production by a manufacturer, a marketing decision, or increased use patterns for drug products. Changes in production can be caused by a shortage of raw materials, damage to a production plant, or, most often, quality-control problems that cause the FDA to stop production. Voluntary or mandatory recalls can cause havoc when there are few and/or less desirable alternatives. An example of a marketing decision causing a shortage is when a manufacturer stops making a rarely used and unprofitable product. Increased use of a drug can cause a shortage when new information stimulates prescribing for a particular "new" indication. Production may not be able to meet this new demand.

When word spreads that a critical drug is in short supply, it just makes matters worse. A drug in short supply becomes harder to obtain than plywood when a hurricane is bearing down on Florida. Managing this natural tendency to "hoard" drugs in short supply is a reason that the FDA has gotten involved in the issue of drug shortages.

The FDA considers a drug shortage to exist only when the drug is "medically necessary" and not when a patient inconvenience alone exists. Anyone can report a shortage to the FDA by calling (888) INFOFDA or (888) 463-6332. More information on the FDA's shortage program can be found on the Internet at www.fda.gov/cder/drug/shortages.

The FDA may take many different steps to help resolve a drug shortage. If the shortage was caused by a manufacturer's noncompliance with quality-control standards, the FDA may weigh the risks of the "noncompliant" drug product with the risk of not having drug to treat a condition. They may facilitate the importation of a foreign source of a drug product when they can ensure the foreign manufacturer meets adequate quality control standards.

The FDA may work with the National Organization for Rare Disorders when a drug manufacturer stops making a drug for marketing reasons. A large manufacturer may not be interested in a drug with $10 million in sales, while a small company may find this "market" attractive.

The FDA (and some manufacturers) have tried to address the effect that hoarding has on shortages. The FDA encourages the establishment of limited access programs that release drugs only based on specified criteria. These criteria may be based on the amount that can be obtained at 1 time or based on the reason that the patient needs the drug.

The Shands Pharmacy intranet website keeps current information on drug shortages. This site can be accessed from the main Pharmacy Website (http://intranet.shands.org/pharm/menu.htm) by using the Shortage link on the left side of the page under the Formulary heading. The direct link to this page can be bookmarked at http://intranet.shands.org/pharm/shortagexl.htm. This site provides the current status of drug shortages at Shands at UF and, in some cases, recommends alternative therapies.

More detailed information about drug shortages and therapeutic alternatives can be found on the American Society of Health System Pharmacists' (ASHP) Drug Shortage Resource Center (http://www.ashp.com/shortage). This website provides important information on the implication of the shortage on patient care.

For example, like all hospitals, Shands at UF still is experiencing a shortage of methylprednisolone injection. The ASHP gives equivalent dosages of the available corticosteroids that can be used in place of methylprednisolone injection. It also reminds prescribers that oral methylprednisolone is available as an option for patients who can take oral medication.

PRESCRIBING

Beta-blockers in airway disease?

Beta-adrenergic antagonists (beta-blockers) are used widely for the treatment of systemic hypertension, other cardiovascular diseases, and noncardiac conditions. Although "beta-blockers" are avoided in patients with reactive airway disease, selective beta-blockers and alpha-beta blockers may be used in some circumstances.

The beta-adrenergic system has beta-1 and beta-2 receptors. Beta-1 receptors are located primarily in the heart, and beta-2 receptors are located primarily in the lungs. Stimulation of the beta-1 receptors results in an increase in heart rate and force of cardiac contraction whereas stimulation of the beta-2 receptor results in bronchodilation.[2]

Animal studies show that absolute separation of beta-1 and beta-2 receptors in organs does not exist. The airways possess both beta-1 and beta-2 receptors.[1] Like most receptors, the distribution of beta-receptors is complicated. Selectivity is not absolute.

Beta-blockers are often classified based on their selectivity for beta-1 and beta-2 receptors. Non-selective beta-blockers (ie, propranolol, sotalol, nadolol, timolol, pindolol, carteolol, and penbutolol) block both beta-1 and beta-2 receptors. Cardioselective beta-blockers (ie, atenolol, metoprolol, bisoprolol, esmolol, acebutolol, celiprolol, and betaxolol) are more selective for the beta-1 receptor. These agents may, however, have some affinity for beta-2 receptors on airway smooth muscle.[1] Higher doses of the cardioselective agents result in the loss of selectivity.[3]

Despite the many benefits of beta-blockers, physicians are often hesitant to prescribe these agents to patients for common conditions because of concerns about possible adverse events. Most reviews state that treatment with beta-blockers is contraindicated in patients with asthma and chronic obstructive pulmonary disease (COPD) due to the reports of acute bronchospasm that occurred with the use of non-cardioselective beta-blockers.

Bronchospasm should be less of a problem with the cardioselective agents since these agents have over 20 times more affinity for beta-1 receptors than for beta-2 receptors. Therefore, there is a theoretical advantage of a cardioselective beta-blocker over a nonselective beta-blocker for the treatment of hypertension in a patient with asthma or COPD.[3]

There have been clinical trials done to evaluate the effects of various beta-blockers on the parameters of pulmonary function. Some of the drawbacks of these studies are that they involved small numbers of patients over short periods of time. The most frequently used beta-blockers in these trials were atenolol, bisoprolol, celiprolol, metoprolol, and pindolol.

There have also been studies that evaluated the differential effects of a cardioselective and a nonselective beta-blocker on pulmonary function in patients with asthma or COPD. The literature supports the theory that cardioselective beta-blockers exert less of an effect on pulmonary function than nonselective beta-blockers in patients with reversible airway diseases but many agents lose their cardioselectivity at higher dosages.

Most of the respiratory adverse events that have been reported with beta-blockers have been in patients with reversible airway disease. This suggests that beta-blockers should be avoided in patients with a history of reactive airway disease unless the patient does not tolerate any other class of antihypertensive. In such case, a cardioselective beta-blocker may be initiated while maintaining optimal treatment with bronchodilators.[3]

◆

Alpha-beta-blockers effectively treat hypertension without exacerbating already compromised pulmonary function in patients with COPD or asthma.

A recent Cochrane review studied 19 homogeneous randomized, blinded, controlled trials that looked at the use of several cardioselective beta-blockers in patients with COPD. The beta-blockers used in these studies were atenolol, metoprolol, bisoprolol, practolol, celiprolol, and acebutolol. These data suggest that the use of cardioselective beta-blockers in patients with COPD has no major adverse effects on FEV1, respiratory symptoms, or response to beta-2 agonists even in those with severe chronic airways obstruction.

In addition, when cardioselective beta-blockers are given to patients with COPD, it appears that these agents do not produce a significant short-term reduction in airway function or in the incidence of COPD exacerbations. However, these agents should be used with caution and be monitored carefully because the trials performed to date have not been long enough to detect an increase in exacerbations. Also, there are no data on the effect of beta-blockers during acute exacerbations.[4]

Beta-blockers that also block alpha-adrenergic receptors have also been studied. Labetalol is a representative of this class. Labetalol is an antihypertensive agent that blocks both alpha-1-, beta-1-, and beta-2 adrenergic receptors at end organs. Labetalol also exerts beta-2 agonist activity on the smooth muscles of the airways and vasculature in experimental animals.[5] Even though the other beta-blockers may cause bronchoconstriction in patients with asthma or COPD, labetalol does not induce bronchoconstriction.

Labetalol has been shown to be effective in the treatment of hypertension in patients with asthma and COPD. Thus, alpha-beta-blockers effectively treat hypertension without exacerbating already compromised pulmonary function in patients with COPD or asthma. This conclusion is based mostly upon well-designed, double-blind, randomized, controlled studies of a limited number of patients.[3]

In conclusion, beta-blockers can cause bronchospasm in patients with reversible airway disease. However, studies have shown that this occurs much less frequently with cardioselective beta-blockers compared to nonselective beta-blockers. In addition, bronchospasm is not seen with mixed alpha-beta blockers. Therefore, these agents may be used in some patients who have COPD or asthma who have failed other agents. If these agents are used, they should be started at low doses and be carefully monitored.

By Brian Kelly, PharmD

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POLICIES AND PROCEDURES

Allowing patients' own medications

Ideally, Shands' Pharmacy would provide all patient medications while patients are hospitalized. However, because many of our patients are here only for a short referral, it may not always make sense to change a patient's drug regimen. The *Formulary* has a limited number of options available. One option for these short referrals is to allow these patients to use their own medications when the drug is not listed in the *Formulary*. The P&T Committee approves the policy under which patients can use their own "home" medications.

Patient safety is always the most important factor in allowing patients to use their own medications. Oral solid dosage forms are allowed, if the medication is in a labeled prescription bottle and a pharmacist has verified the contents. The prescribing physician must write a specific order for the "home" medication, specifying the drug and dosage and that the patient may use their own medication. Like all medications, these medications are listed in the patient's medication profile. This allows for appropriate safety screening for dosage, therapeutic duplication, drug interactions, etc.

In general, oral solid dosage forms are acceptable. However, patients cannot continue their own controlled substance. These drugs are stored with the patient's valuables or sent home with the patient's family.

Parenteral medications are a concern. For example, intravenous medications have a greater potential for contamination or potency problems. Unfortunately, there is a growing list of parenteral medications that are available only through limited distribution programs.

Shands cannot stock a medication that is available only through limited distribution programs. These medications are impossible to list in the *Formulary*. Only the patient has a supply. For example, the new injectable drug used to treat patients with HIV, enfuvirtide (Fuzeon®), cannot be purchased for inpatient use. If a patient is admitted on enfuvirtide, they must continue to take their own medication. Parenteral medications that are only available from limited distribution networks can be used in the hospital. A pharmacist has to examine the medication to assure its identification.

Some parenteral medications are specialty dosage forms for administration by specific devices (eg, insulin cartridges for subcutaneous insulin pumps). The revised policy states, "as a general rule, injectable medications will be supplied by the Pharmacy. Exceptions to this policy will be made by pharmacy administration staff based on circumstances associated with restricted medication distribution programs, specific patient care requirements, and assessment of risk and alternatives." Epoprostenol, insulin, treprostinil, or similar drugs that are administered via patients' own infusion devices are examples of acceptable parenteral medications.

Recently, the P&T Committee made an exception to this policy for ophthalmic medications. The wide variety of ophthalmic drugs and combinations, as well as the critical nature of these drugs made allowing patients to use their own medication a benefit compared with the risks.

Patients' own metered-dose inhalers (MDIs) are also allowed for inpatient use in the revised policy. The probability of product problems with these agents is very low.

Patients cannot use their own compounded medications. Compounded medications can be used in the hospital only under a previously approved policy that requires that the vendor meet quality standards.