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Drugs & Therapy BULLETIN

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met October 15, 2002. 2 drugs or dosage forms were added in the *Formulary* and 1 drug was deleted. 1 drug was evaluated, but not added.

◆ **ADDED**

Bosentan
(Tracleer® by Actelion)

Lidocaine Cream 4%
(ELA-Max® by Ferndale Laboratories)

◆ **DELETED**

Tubocurarine (generic)

◆ **EVALUATED, BUT NOT ADDED**

Hetastarch 6% in Lactated Ringers
(Hextend® by Abbott)

Bosentan is an endothelin antagonist that is an oral alternative to intravenous epoprostenol (Flolan®) for the treatment of pulmonary hypertension. Until recently, bosentan could not be considered for formulary addition because it could not be stocked in the hospital. When the distributors of bosentan changed this policy, it was added in the high-priority nonformulary list. In keeping with the new nonformulary policy, bosentan was evaluated as soon as possible.

The 75% of patients with pulmonary hypertension who do not respond to calcium channel blockers, like nifedipine, are treated with intravenous epoprostenol or oral bosentan. Bosentan's labeled indication is for the treatment of pulmonary arterial hypertension in patients with World Health Organization (WHO) Class III and IV symptoms, to improve exercise ability and decrease the rate of clinical worsening.

(continued on next page)

PRESCRIBING

Writing prescriptions for controlled substances

Recent news reports highlight cases where prescriptions have been forged or altered to get access to controlled substances. When these incidents are reported, it stresses the fact that prescribers must be diligent to minimize forgeries and altered prescriptions.

The diversion and abuse of pharmaceutical controlled substances is a multi-billion dollar illicit market in the United States. In 1997, 15 of the top 20 abused drugs reported in the Drug Abuse Warning Network were pharmaceutical controlled substances. Benzodiazepines (eg, alprazolam, clonazepam, diazepam) are high on this list as are opioids and opioid combinations.

A common scam used to get increased access to controlled substances is to alter the quantity on a prescription. For example, a prescription for #60 Vicodin is altered to appear to be #160 Vicodin—ie, a "1" is inserted in front of the 60. Pharmacists are often suspicious of unusual quantities; so do not be surprised when you get a call from a pharmacist when you prescribe an unusual quantity or any quantity over 100. Another scam is to change the strength of a drug. A prescription for OxyContin 10 mg can be altered easily to OxyContin 40 mg. Writing the words describing the quantity and strength (ie, #60 [sixty] OxyContin 10 [ten] mg) can prevent altered prescriptions.

The Drug Enforcement Agency (DEA) recommends that pharmacists contact the prescriber when anything looks unusual. If pharmacists think a prescription is forged, altered, or counterfeited, the DEA instructs pharmacists to call their local police before it is dispensed.

Prescribers can avoid telephone calls and possible problems for their patients by writing the quantity as well as writing the numeral for both the quantity and the strength. This approach is like writing a check, where the written description of the quantity can be compared to the number quantity. This simple approach can help avoid altered prescriptions and let pharmacists know when unusual quantities are legitimate.

Prescribers have a personal responsibility to protect against drug diversion. The DEA recommends that quantities for controlled substances should always be limited. Of course, prescribers of controlled substances must have their DEA registration number on the prescription. Since 2001, the State of Florida has required prescribers to use counterfeit-proof prescriptions pads for all patients covered by Medicaid. These prescriptions blanks prevent photocopying or scanning of prescriptions that would allow them to be altered.

Some states have cumbersome duplicate or triplicate prescription pads for controlled substances. These systems are of questionable value. Other states electronically monitor patterns of prescribing when these prescriptions are processed at pharmacies. Electronic monitoring may decrease diversion, but reducing diversion still takes vigilance from prescribers and pharmacists. The best method of verification is still directly from the prescriber. If you receive a call about a questionable prescription, please be understanding.

INSIDE THIS ISSUE

Formulary update, *from page 1*

The main published trial with bosentan showed a significant improvement in the 6-minute walking test in patients with primary pulmonary hypertension or pulmonary hypertension associated with connective-tissue disease. Patients had less dyspnea and could walk farther. Patients also had a lower death rate, less hospitalization, and fewer other markers of clinical worsening. These effects were maintained for 7 months on follow-up. Pulmonary artery pressures were not significantly decreased.

Bosentan should be initiated at 62.5 mg twice a day for 4 weeks. The dosage can then be increased to the maintenance dosage of 125 mg twice a day. Dosages above 125 mg twice a day do not appear to confer additional benefit sufficient to offset the increased risk of liver injury.

Bosentan has the potential to cause serious liver injury and dosage adjustment is critical with elevated liver function tests. Bosentan can cause major birth defects and documentation that a patient is not pregnant is critical. Because bosentan is metabolized by CYP 2C9 and 3A4, drug interactions are important.

In the outpatient setting, only a limited distribution network can dispense bosentan. These specialty pharmacies verify liver function tests and pregnancy tests before the supply of bosentan is dispensed.

Bosentan costs approximately $50 a tablet in the inpatient setting. The financial impact is unknown; however, if used appropriately, the only appropriate alternative is epoprostenol, which is more expensive.

The use of bosentan in conditions besides primary pulmonary hypertension or secondary pulmonary hypertension associated with connective tissue disease is controversial. Bosentan may cause patients with heart failure to deteriorate; thus, appropriate patient selection is important.

Lidocaine cream 4% is ELA-Max®. ELA-Max® 4% is an over-the-counter (OTC) product with a labeled indication for temporary relief of pain associated with minor cuts and abrasions of the skin, minor burns, including sunburn, minor skin irritation, and insect bites. ELA-Max® was considered for addition in the *Formulary* as an alternative to EMLA (Eutectic Mixture of Local Anesthetics [lidocaine-prilocaine]) cream to decrease pain associated with IV cannulation or blood draws in children.

ELA-Max® is promoted as working faster than EMLA cream. EMLA cream takes about an hour to be effective. Because ELA-Max® is in a lipid vehicle, it may work more quickly (ie, 30 minutes).

The published studies comparing EMLA and ELA-Max® in children undergoing venipuncture show that these agents are equivalent. The authors of 1 study suggest that there was a trend for lower pain scores with ELA-Max®. This study did not show a benefit of occlusion when applying ELA-Max®.

ELA-Max® costs approximately 10% less than EMLA. EMLA cream was not removed from the *Formulary*. After approximately 6 months, the formulary status of ELA-Max® and EMLA will be reconsidered.

Beginning November 15th and through approximately mid-2003, the only distribution of EMLA Cream will be directly from AstraZeneca to hospitals. It will be restricted to inpatient use only. The Consumer Product Safety Commission (under the Poison Prevention Act) recently passed a rule requiring child-resistant packaging. After January 1, 2003, EMLA cream cannot be dispensed for use outside the hospital in a non-child-resistant package. Therefore, EMLA cream will not be distributed to any clinic during this period.

This rule applies to any product containing more than 5 mg of lidocaine in a single package, so it would also apply to lidocaine ointment, jelly, or viscous lidocaine in non-child-resistant packaging. ELA-Max® is an OTC product and the 30-gram tube is already in a child-resistant package.

Tubocurarine was a long-acting neuromuscular blocking agent used to relax skeletal muscles as an adjunct to general anesthesia. Tubocurarine was also used to diagnose myasthenia gravis when tests with edrophonium or neostigmine gave inconclusive results.

Unfortunately, tubocurarine has been discontinued by all manufacturers (eg, Lilly, Abbott, Geneva) because of a raw material shortage. We have not dispensed Tubocurarine for over 2 years. Alternative neuromuscular blocking agents with similar onset times and durations of action exist (eg, atracurium, doxacurium, and pancuronium).

Hetastarch 6% in lactated ringers (LR) is Hextend®. The proposed advantage of hetastarch in LR versus hetastarch in normal saline (NS) is less adverse effects—specifically less CNS confusion post cardiopulmonary bypass and/or less bleeding.

Hetastarch in NS is listed in the *Formulary*. Whether there is sufficient evidence to conclude that a difference exists that justifies the 60% increased cost of hetastarch in LR versus hetastarch in NS is an issue. Currently, there are no published data to support increased efficacy.

There are few data that suggest better safety, but these are based on surrogate markers. There are no documented differences in adverse outcomes between hetastarch in LR compared to hetastarch in NS. In the Hextend® labeling it states that there are no significant differences in the number of adverse or serious adverse events between Hextend® and hetastarch in NS.

A published study found a trend towards less blood loss during major surgery, but these differences were not statistically significant. Another study found that laboratory markers for metabolic acidosis were better in the Hextend®-treated patients compared with hetastarch in NS in elderly patients undergoing major surgery. Also, gastric mucosal perfusion was improved. However, these differences did not translate to poorer outcomes in this small (47-patient) study.

Another study used laboratory markers for coagulation status (eg, thromboelastography) to conclude that Hextend® had less effect on coagulation. However, there was no difference in the use of blood, fresh frozen plasma, or cryoprecipitate use. Blood loss was also not found to be different.

Therefore, the P&T Committee concluded that there was insufficient evidence to add Hextend® in the *Formulary* at this time. Even if Hextend® were the same cost as hetastarch in NS, there are logistical issues with its use. If both hetastarch in LR and NS are available, it could increase the chances for medication errors. Nursing staff could choose the wrong product. If only Hextend® were available, patients with orders for hetastarch in NS would likely be given Hextend® instead. Therapeutic interchange is not an option because of the logistics of the dispensing of hetastarch.

If additional data become available that show an advantage for Hextend® and/or the cost is lowered, Hextend® can be reconsidered. However, the logistical issues and potential for medication errors would still need to be addressed.

Changes made in the *Charity Care Formulary*

The *Charity Care Formulary*, which is also known as "The 9 Plan," was established in 1995. It is a short list of drugs that are either inexpensive or easy to obtain from manufacturers. Since not all drugs can be listed, priority is given to agents that will help keep patients out of the hospital. Currently, there are less than 150 drugs listed in the *Charity Care Formulary*. Hopefully, this program offers patients some inexpensive options without being so expensive the hospital could not continue to fund it.

Patients qualify for the *Charity Care Formulary* by meeting geographic restrictions, by having a household income at or below the 150th percentile of the federal poverty guidelines, and by being current patients at Shands at the University of Florida. This only applies to the 1600 SW Archer Road and the Shands Medical Plaza (ie, 2000 SW Archer Road) locations. Patients must provide documentation of their residence and income in order to qualify. Most patients who qualify are elderly patients who have Medicare coverage for their healthcare, but who have difficulty paying for their prescriptions. More information on the eligibility requirements for the *Charity Care Formulary* can be found on the Shands intranet at http://intranet.shands.org/pharm/outpatie.htm.

There have not been significant changes in the *Charity Care Formulary* for many months. Several changes in the drugs listed were made to keep this program viable. Most additions provide inexpensive options. These are often generic alternatives to inexpensive brand-name drugs. Several deletions were also made. Most of these deletions were because of lack of use; however, some were because companies' access programs have become too difficult or there are equally effective, less expensive alternatives that are now available.

A complete list of drugs listed in the *Charity Care Formulary* can be found on the Shands intranet at http://intranet.shands.org/pharm/ccform.htm. Drugs are listed in 37 different categories. By selecting a category, a prescriber can determine what options are available. For example, ACE inhibitors is the first category. By selecting this category, a prescriber could choose from enalapril, lisinopril, or quinapril.

A complete list of the additions and deletions made to the *Charity Care Formulary* is listed in the table.

CHARITY CARE FORMULARY CHANGES

	Drug	Category
ADDED	Chlorpheniramine	Antihistamines
	Chlorpheniramine + Pseudoephedrine	Antihistamines
	Clonidine	Alpha Blockers
	Diphenhydramine	Antihistamines
	Enalapril	ACE Inhibitors
	Fluoxetine	Antidepressants
	Glucose test strips (One Touch Ultra®)	Diabetes Agents
	Glucose monitor (One Touch Ultra®)	Diabetes Agents
	Hydrochlorothiazide	Diuretics
	Hydrocodone + Acetaminophen	Analgesics
	Hydroxyzine	Antihistamines
	Isosorbide mononitrate	Nitrates
	Levothyroxine (Levoxyl®)	Thyroid Medications
	Metoprolol ER (Toprol® XL)	Beta Blockers
	Morphine ER (MS Contin®)	Analgesics
	Nadolol	Beta Blockers
	Naproxen	NSAIDs
	Naproxen Enteric-Coated	NSAIDs
	Oxycodone	Analgesics
	Rosiglitazone (Avandia®)	Diabetes Agents
	Salsalate	NSAIDs
	Sulfasalazine	GI Drugs
	Sulindac	NSAIDs
	Trazodone	Antidepressants
	Warfarin (generic)	Anticoagulants
DELETED	Beclomethasone inhaler	Miscellaneous
	Betaxolol	Beta Blocker
	Cetirizine	Antihistamines
	Disopyramide	Antiarrhythmics
	Hydrocortisone injection (Solu Cortef®)	Adrenals
	Levothyroxine (Synthroid® brand)	Thyroid Medications
	Ramipril	ACE Inhibitors
	Verapamil ER (Covera HS® brand)	Calcium Channel Blockers
	Warfarin (Coumadin® brand)	Anticoagulants

Synthroid® brand of levothyroxine was deleted from the Thyroid Medications category of the *Charity Care Formulary*. Because of therapeutic equivalency and lower cost, Levoxyl® is now listed. Because levothyroxine is listed in the State of Florida's Negative Formulary, interchange will not be automatic. The Negative Formulary is a short list of medications that cannot be generically interchanged in the State of Florida. These drugs include digitoxin, conjugated estrogens, dicumarol, oral solid dosage forms of chlorpromazine, theophylline extended-release, levothyroxine, and pancrelipase. Prescribers will be contacted to switch brands of levothyroxine. Patients will have to pay the difference if the lower cost alternative cannot be used.

All other generic interchanges, including warfarin, will be done without contacting the prescriber.

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