

Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met February 19, 2013. 1 drug was added in the *Formulary*, 2 drugs were deleted, and 7 drugs were designated nonformulary and not available. 5 drugs had criteria for use changes.

◆ ADDED

Amoxicillin-Clavulanate Suspension
(generic Augmentin® ES)

◆ DELETED

Aluminum Sulfate-Calcium Acetate (Domeboro® Powder)*
*Nonformulary and not available

Hydromorphone 3-mg Suppositories (Generic)*
*Nonformulary and not available

◆ NONFORMULARY AND NOT AVAILABLE

Lomitapide (Juxtapid®)†
†Patients must use their own supply

Loxapine Inhalational Powder
(Adasuve®)

Sodium, Potassium & Magnesium Sulfate with PEG 3350 & Electrolytes (Suclear® Kit)

Sumatriptan Nasal Spray
(Imitrex®)

Sumatriptan Transdermal
(Zecuity®)

◆ CRITERIA-FOR-USE CHANGES

Dabigatran (Pradaxa®)‡
‡Restricted: cannot be used with mechanical heart valves

Fluconazole Liquid (Generic)‡
‡Dose rounding modified

Levothyroxine IV (Generic)‡
‡Added to IV to PO policy (1:2 ratio)

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PRESCRIBING

Why isn't hydrocodone listed in the *Formulary*?

This is a common question at Shands at UF. Why can't I prescribe hydrocodone for pain for my inpatients? Hydrocodone is one of the most commonly prescribed pain drugs in the outpatient setting. Three of the top 20 drug prescriptions dispensed in 2011 were hydrocodone with acetaminophen products (ie, #1 Watson with 59 million prescriptions filled, #2 Mallinckrodt 46 million, and Qualitest 25 million).¹ With codeine at least temporarily unavailable for use, hydrocodone appears to be a possible alternative for pain.

We do not allow patients to use their own supply of controlled substances. Patients' own controlled substances are sent home with family members or stored with patient's valuables until their discharge.

Most people think of the common brand names for hydrocodone with acetaminophen like Vicodin® or Lortab®, but there are many generic products containing varying amounts of hydrocodone (from 2.5 mg to 10 mg) and acetaminophen. These fixed-dose combinations lack flexibility in adjusting the dose of hydrocodone when pain is increasing. Stocking various combinations of hydrocodone with acetaminophen would be expensive (controlled substance storage is expensive), could lead to errors, and is impractical.

Hydrocodone is a semi-synthetic opioid similar in strength to codeine. Hydrocodone does not have any therapeutic advantages compared with other opioids. Like codeine, it is metabolized by CYP2D6.² Hydrocodone is metabolized to hydromorphone (Dilaudid®), a more potent (10-33 more potent) opioid.³ Unlike codeine, CYP2D6 metabolic status does not appear to affect the magnitude of response to hydrocodone. Hydrocodone is active and does not have

to be converted to an active metabolite. Further, as the amount of the hydromorphone metabolite goes up, the amount of parent compound [hydrocodone] goes down. There is currently insufficient evidence to conclude that pain relief decreases with poor metabolizers or that there is increased risk with ultra-rapid metabolizers...at least right now.³

The real advantage hydrocodone-acetaminophen combinations have over other opioid-acetaminophen combinations is their controlled substance schedule status. Since hydrocodone-acetaminophen combinations are in Schedule III [federally and in Florida], they are more convenient for outpatient use. Schedule III controlled substances can be telephoned or faxed to a community pharmacy. Up to 6 months of refills can be authorized.

These advantages are not relevant in the inpatient setting. Hydrocodone products have been nonformulary and not available for use at Shands UF since 1991. They were not available prior to that, but the 1991 designation formalized that decision. Before 1991, patients and prescribers asked to continue their home therapy upon admission. Nonformulary controlled substances have always been problematic.

Most patients admitted on hydrocodone-acetaminophen are switched to oxycodone-acetaminophen. Other pain drugs could be used (eg, acetaminophen alone, tramadol, nonsteroidal anti-inflammatory drugs) instead. When genetic testing for codeine becomes available, codeine-acetaminophen will

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INSIDE THIS ISSUE

◆ NSAID failure

◆ CRITERIA-FOR-USE CHANGES

Ponatinib (Iclusig®)‡

‡Added in the Chemotherapy Policy; Nonformulary Drug

Voriconazole (Generic)‡

‡Expanded prophylactic use in the BMT Unit

Augmentin® is a fixed combination of the aminopenicillin amoxicillin and the beta-lactamase inhibitor **clavulanate**, which extends amoxicillin's activity against organisms that produce beta-lactamase. **Augmentin**® ES (amoxicillin-clavulanate 600 mg/42.9 mg per 5 mL) is an "extra strength" version of amoxicillin-clavulanate with more amoxicillin to optimize coverage for *Streptococcus pneumoniae*. A dose of 90 mg per kilogram per day of amoxicillin is preferred for *Streptococcus pneumoniae*. The original Augmentin® has a ratio of 7:1 of amoxicillin to clavulanate, while the ES formulation has a 14:1 ratio.

Since 2002, the practice at Shands UF was to combine 2 formulations to achieve proper amoxicillin and clavulanate concentrations when prescribing high-dose amoxicillin-clavulanate therapy. Orders for Augmentin® ES were changed to regular Augmentin® with a supplemental dose of amoxicillin. Augmentin® provides 45 mg/kg/day of amoxicillin, which was supplemented with an additional 45 mg/kg/day of amoxicillin. Augmentin® ES has shown both clinical and bacteriologic efficacy in clinical trials for acute otitis media in children.

Although using 2 products has a slight cost advantage over the commercially available product, it can also cause confusion upon discharge. The Anti-Infective Subcommittee recommends Augmentin® ES oral suspension for the treatment of recurrent or persistent acute otitis media or empirically for children with recent antibiotic exposure, age greater than or equal to 2 years, or who attend daycare regularly.

There are insufficient data available to recommend the ES-formulation in adults and the current susceptibility testing for anaerobes and Enterobacteriaceae do not use the 14:1 amoxicillin-clavulanate ratio. Therefore, *in-vitro* testing will not serve as an adequate surrogate for treating pathogens outside of those associated with respiratory, sinus, or otic infections.

Domeboro® is a combination of **aluminum sulfate and calcium acetate** used topically as an astringent and antibacterial. Aluminum sulfate

[only] is Burow's solution. Domeboro® is considered a "modified" Burow's solution. It is rarely used. Records show it was not used in the last year. Therefore, Domeboro® Powder was deleted from the *Formulary* and designated "not available."

Hydromorphone suppositories are rarely used and were deleted from the *Formulary* and designated nonformulary and not available. This decision was supported by the pain service.

Hydromorphone suppositories pose a difficult distribution dilemma because they are a controlled substance that should be refrigerated. They are not stable outside of a refrigerator.

Lomitapide is a microsomal triglyceride transfer protein inhibitor with a labeled indication as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).

HoFH is a rare inherited condition that makes the body unable to remove LDL-C from the blood, causing abnormally high levels of circulating LDL-C. In the United States, HoFH occurs in approximately one in one million individuals. For those with HoFH, heart attacks and death often occur before age 30. Lomitapide works by impairing the creation of the lipid particles that ultimately give rise to LDL-C.

Lomitapide is a capsule taken once a day, without food, and at least 2 hours after the evening meal. Patients should take supplements that contain fat-soluble vitamins and essential fatty acids daily while taking lomitapide.

The safety and efficacy of lomitapide were evaluated in a clinical trial of 29 patients with HoFH. On average, levels of LDL-C fell by approximately one-half during the first 26 weeks among those who tolerated the drug. Lomitapide carries a boxed-warning regarding a serious risk of liver toxicity because it is associated with liver enzyme abnormalities and accumulation of fat in the liver, which could potentially lead to progressive liver disease with chronic use. Lomitapide also reduces the absorption of fat-soluble nutrients and interacts with several other drugs.

The FDA approved lomitapide with a Risk Evaluation and Mitigation Strategy (REMS) to promote safe use including prescriber and pharmacy certification and documentation of safe-use conditions consisting of a prescription authorization form that will be required to accompany each new prescription.

The FDA is requiring 3 postmarketing studies for lomitapide: an animal study to evaluate the potential for toxicity in children and teens; a long-term registry of patients with HoFH treated with lomitapide to determine the long-term safety; and an enhanced pharmacovigilance program to monitor reports of malignancy, teratogenicity, and hepatic abnormalities.

The most common adverse reactions in the clinical trial included diarrhea, nausea, vomiting, indigestion, and abdominal pain.

According to news reports, Juxtapid® will cost about \$250,000 per year, continuing the trend of very high costs for drugs with an expected narrow use (ie, orphan drugs).

Lomitapide was designated a nonformulary and not available drug; patients must use their own supply if they are hospitalized.

Loxapine is a conventional anti-psychotic that was approved in 1975 for the treatment of schizophrenia. Adasuve® is an **inhalational powder** form of loxapine with a labeled indication for the acute treatment of agitation associated with schizophrenia or bipolar disorder in adults. The approval of Adasuve® was based on two phase-III trials, but approval was delayed several times. Loxapine inhalational powder was designated nonformulary and not available.

Suclear® is a combination osmotic laxative with a labeled indication for cleansing the colon in preparation for colonoscopy in adults. This colonoscopy "prep" is given as 2 separate doses by 2 possible methods (ie, "split-dose (2-day) regimen" or "day-before" regimen).

Suclear® Kit contains an oral solution that is a combination of **sodium sulfate, potassium sulfate, and magnesium sulfate** in a 6-ounce bottle that is diluted to 16 ounces in a [provided] mixing container with cool water. The entire 16 ounces is consumed within 20 minutes. The 16-ounce container is refilled with water and consumed within 2 hours. The container is refilled with water and consumed before going to bed with the split-dose method.

The kit also contains polyethylene glycol (PEG) 3350 with electrolytes, which is available as a 2-liter jug with powder (**PEG-3350, sodium chloride, sodium bicarbonate, and potassium chloride**) that is reconstituted with cool water before use. This part of the kit is similar to GoLyteLy®, except it is half the volume (2 liters versus 4 liters).

After shaking the PEG 3350 with electrolytes jug to dissolve all the

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powder, it is consumed with or without a flavor pack. The 2 liters of fluid is consumed before the colonoscopy on the day of the procedure for the split-dose method. A 16-ounce container is consumed every 2 hours before the procedure [up to 2 hours before the procedure]. There are four 16-ounces doses, which could take up to 8 hours to complete the regimen.

For the split-dose method, the sodium-potassium-magnesium sulfate mixture is given the day before the procedure, and the PEG with electrolytes mixture on the day of the procedure. The day-before method gives sodium-potassium-magnesium sulfate mixture first, then follows with the PEG with electrolytes starting 2 hours after the sodium-potassium-magnesium sulfate mixture.

This colonoscopy “prep” does not appear to offer any advantage over other products; therefore, it was designated nonformulary and not available.

Zecuity® is a **transdermal** form of the migraine drug **sumatriptan**. Zecuity® is a single-use “patch” that delivers sumatriptan through a mild, battery-powered electrical current. It has a labeled indication for the acute treatment of migraine with or without aura. Sumatriptan is already available by several dosage forms (eg, subcutaneous injection, oral tablet, nasal spray). Sumatriptan subcutaneous injection and oral tablets are listed in the *Formulary*.

The potential advantage of Zecuity® is that a dose of sumatriptan can be delivered “quickly” through the skin in patients who cannot take oral drugs and are unable or unwilling to administer a subcutaneous injection. There is an auto-injector form of subcutaneous sumatriptan (Alsuma®), which has previously been designated nonformulary and not available for inpatient use. In the inpatient setting, a nurse-administered subcutaneous injection of sumatriptan is the preferred alternative in patients who cannot take oral drugs.

A review of sumatriptan products listed in the *Formulary* revealed that **sumatriptan nasal spray** had never been reviewed. Like Zecuity®, this dosage form is not needed in the inpatient setting.

Therefore, transdermal sumatriptan and sumatriptan nasal spray (eg, Imitrex® Nasal Spray) were designated nonformulary and not available. Patients can use their own supply or receive a subcutaneous injection of sumatriptan.

Dabigatran is the first oral direct thrombin inhibitor approved with a labeled indication to reduce the risk of stroke and systemic embolism in patients with *non-valvular* atrial fibrillation. It is an alternative to warfarin in this patient population

The FDA issued a notice informing healthcare professionals and the public that dabigatran should not be used to prevent stroke or other major thromboembolic events in patients with mechanical heart valves, also known as mechanical prosthetic heart valves. A clinical trial in Europe (the RE-ALIGN trial) was recently stopped because dabigatran users were more likely to experience strokes, heart attacks, and blood clots forming on the mechanical heart valves than were users of the anticoagulant warfarin. There was also more bleeding after valve surgery in the dabigatran users than in the warfarin users.

Dabigatran is not approved for patients with atrial fibrillation caused by heart valve problems. The FDA is requiring a contraindication of dabigatran in patients with mechanical heart valves in its labeling. Healthcare professionals should promptly transition any patient with a mechanical heart valve who is taking dabigatran to “another anticoagulant.” The use of dabigatran in patients with another type of valve replacement made of natural biological tissue, known as a bioprosthetic valves, has not been evaluated and cannot be recommended. Patients with all types of prosthetic heart valve replacements taking dabigatran should talk to their healthcare professional as soon as possible to determine the most appropriate anticoagulation treatment. Patients should not stop taking anticoagulants without guidance from their healthcare professional; stopping dabigatran or other anticoagulants suddenly can increase the risk of blood clots and stroke.

A question will be placed in Epic to ask prescribers if patients have mechanical heart valves and prevent its use in the patient population. Warfarin with possibly a bridge with heparin or a low molecular weight heparin is an alternative.

Fluconazole is a triazole antifungal that has been listed in the *Formulary* since 1990. It is ordered on a milligram-per-kilogram basis in children, which often leads to irregular doses, some of which are difficult to measure. For many years, we have rounded doses in children to 12 dose intervals.

Shands Jax requested that Shands UF adjust our fluconazole oral liquid dose standardization to be more conservative. The “old” SUF fluconazole

rounding policy allows as much as a 33% change when rounding to 1 of 12 doses (ie, from 3 mg to 400 mg). The new fluconazole rounding will limit rounding to 25% and would round doses to 1 of 24 doses ranging from 1.5 mg to 400 mg. This change is needed because we share the Epic drug files.

Levothyroxine is a synthetic version of the endogenous thyroid hormone tetraiodothyronine (T4). It is used as replacement therapy for patients with hypothyroidism.

The use of the IV dosage form for levothyroxine appears to be high at Shands UF compared with other similar institutions. This is significant, because the intravenous dosage form is considerably more expensive than the oral form.

There may be 2 reasons for intravenous use. Patients may be receiving the IV dosage form when they could be switched to the oral dosage form for hypothyroidism. Although the exact conversion is debatable, most clinicians double the IV dose when switching to the oral dosage form. This is based on a 50% to 80% bioavailability for oral levothyroxine. Also, the IV dosage form may be used for off labeled uses in critically ill patients.

The P&T Committee approved that IV levothyroxine be added in the IV-to-PO conversion list, with twice the oral dose being substituted for the IV dose of levothyroxine for the treatment of hypothyroidism.

Ponatinib is an oral kinase inhibitor with a labeled indication for the treatment of adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) that is resistant or intolerant to prior tyrosine kinase inhibitor therapy or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) that is resistant or intolerant to prior tyrosine kinase inhibitor therapy.

The FDA reviewed ponatinib under the agency’s priority review program, which provides for an expedited 6-month review for drugs that may provide safe and effective therapy when no satisfactory alternative therapy exists, or offer significant improvement compared to marketed products. Ponatinib targets CML cells that have a particular mutation, known as T315I, which makes these cells resistant to currently approved kinase inhibitors.

Ponatinib’s safety and efficacy were evaluated in a single clinical

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trial of 449 patients with various phases of CML and Ph+ ALL. All participants were treated with ponatinib. The drug's effectiveness was demonstrated by a reduction in the percentage of cells expressing the Philadelphia chromosome genetic mutation found in most CML patients, major cytogenetic response (MCyR). Fifty-four percent of all patients and 70% of patients with the T315I mutation achieved MCyR. The median duration of MCyR had not yet been reached at the time of analysis.

In accelerated and blast phase CML and Ph+ ALL, ponatinib's effectiveness was determined by the number of patients who experienced a normalization of white blood cell counts or had no evidence of leukemia (major hematologic response or MaHR). Results showed: 52% of patients with accelerated phase CML experienced MaHR for a median duration of 9.5 months; 31% of patients with blast phase CML achieved MaHR for a median duration of 4.7 months; and 41% of patients with Ph+ ALL achieved MaHR for a median duration of 3.2 months.

Ponatinib is being approved with a boxed warning alerting patients and healthcare professionals that it can cause blood clots and liver toxicity. The most common adverse effects reported during clinical trials include high blood pressure, rash, abdominal pain, fatigue, headache, dry skin, constipation, fever, joint pain, and nausea.

Ponatinib was added in the Chemotherapy Policy, but remains nonformulary.

Voriconazole is a second-generation synthetic triazole antifungal agent with a broader spectrum of activity against *Aspergillus* species than other azoles. It also causes more significant drug interactions, including interactions with transplant drugs.

Voriconazole is used for empiric therapy for the management of neutropenic fever and the management of probable and documented mold infections including first-line therapy for invasive *Aspergillus* infections.

The criteria for voriconazole use were expanded to include mold prophylaxis in "at risk" populations in the Bone Marrow Transplantation Unit [in place of fluconazole prophylaxis]. At risk populations are defined as patients with AML undergoing re-induction for persistent disease or treated with myeloablative regimens, patients with delayed engraftment (greater than 25 days after HSCT) or acute GVHD on greater than or equal to 1 mg/kg/day of prednisone (or equivalent) for more than 3 weeks; and, patients undergoing HSCT with history of invasive mold infection.

Hydrocodone–Acetaminophen,

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be a good alternative if patients have the “right” genotypes. Hydrocodone is roughly equal to oral codeine or morphine on a mg-per-mg basis and is about 2/3 the potency of oxycodone (ie, 5 mg oxycodone equals 7.5 mg hydrocodone). Thus, 5 mg hydrocodone is slightly less potent than 5 mg oxycodone (ie, roughly equals 3.3 mg of oxycodone).

In 2000, the State of Florida considered changing hydrocodone to Schedule II. The law passed in 2000 [HB2085] was stimulated by a person who illegally sold hydrocodone-acetaminophen and who was not prosecuted because the combination was a Schedule III substance. In 2001, this decision was “partially” reversed. The revision essentially reverted prescribing to Schedule III rules with Schedule II criminal penalties.

Now the Drug Enforcement Agency (DEA) and FDA are considering rescheduling hydrocodone and hydrocodone combination products to Schedule II based on new data that suggests hydrocodone-combination have the same abuse potential as oxycodone-combination.³ Schedule II is for drugs with high potential for abuse, and hydrocodone has demonstrated that it is highly abusable.

If hydrocodone is placed in Schedule II, its primary advantage in the outpatient setting will disappear. An original written prescription would be needed for each refill.⁴ Prescribing up to a 3-months’ supply of hydrocodone would be possible. DEA rules allow up to a 30-day supply per prescription and additional prescriptions for future filling for up to 90 days.⁴ Patients would have to be assessed by the prescriber every 3 months.

Some have proposed that rescheduling will result in increased healthcare costs. It may increase the use of other opioids, like methadone, which could be dangerous if prescribers do not know how to properly dose it. The use of acetaminophen [alone], tramadol, or NSAIDs may also increase if patients can tolerate their chronic use. A schedule change would not affect the use of hydrocodone combinations for acute pain after a procedure.

REFERENCES

1. Bartholow M. Top 200 drugs of 2011. Pharmacy Times. Published online 7/10/2012. Accessed online 2/12/2013 at <http://www.pharmacytimes.com/publications/issue/2012/July2012/Top-200-Drugs-of-2011>.
2. Crews KR, Gaedigk A, Dunnenberger HM, et al. Clinical pharmacogenetics implementation consortium (CPIC) guidelines for codeine therapy in the context of cytochrome P4502D6 (CYP2D6) genotype. *Clin Pharmacol Ther* 2012;91:321-6.
3. FDA briefing document: Drug safety and risk management advisory committee (DSaRM) meeting—January 24-25, 2013. Accessed online at <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM334276.pdf> on February 24, 2013.
4. Code of Federal Regulations, Chapter 11 section 1306.12. Accessed at <http://www.gpo.gov/fdsys/pkg/CFR-2009-title21-vol9/pdf/CFR-2009-title21-vol9-sec1306-12.pdf> on February 24, 2013.

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EVIDENCE-BASED MEDICINE

Alternatives when an NSAID fails?

Some prescribers believe that if one nonsteroidal anti-inflammatory drug (NSAID) does not work, another should be tried. Third-party payers often require failure of 2 different generic NSAIDs before a more-expensive NSAID is recommended. This may be reasonable, but it is not based on high-level evidence. In fact, the limited evidence available suggests that trying the same NSAID again might be just as effective.¹

There are 17 different oral NSAIDs on the market, but very few have been compared head-to-head. No data show that a specific NSAID has superior pain-relieving abilities.² Although there have been reams of data promoting the relative safety of NSAIDs, few objective data prove superiority. In general, NSAIDs are equally effective and all have risks. NSAIDs should be reserved for patients who fail non-drug treatments, acetaminophen, or other pain drugs. Intermittent NSAID use is preferred over chronic use.

The Deputy Center Director for Clinical Science at the FDA recently questioned the long-held assumption that patients respond differently to different NSAIDs.¹ He cites a study showing that patients who failed celecoxib (Celebrex[®])

responded equally to rofecoxib (Vioxx[®]) or celecoxib. Pain relief was similar when nonresponders are randomized to a similar drug or the same drug.

There is an inherent bias when patients who fail a treatment are switched to something new. Without a control group, we will never know if the new treatment is better. We cannot conclude that a different NSAID works better than the failing NSAID without a control group that re-challenges patients to the ineffective NSAID. These studies are rarely done.

Without a control group, the results are biased in favor of the new treatment. If the new treatment fails, it is not a big deal. If the new treatment works, it appears better than it really is. Switch studies are biased to show a change. If a drug that shows good control is switched to a new drug, the failures that occur will be inappropriately blamed on the new drug. If a drug fails, then the patient is switched to a new drug, success is inappropriately attributed to the new drug.

Picking the new NSAID over the old NSAID is similar to problems with the famous *Schlitz* beer challenge commercial

during the 1981 Super Bowl.³ One hundred "loyal" *Michelob* drinkers compared the taste of *Schlitz* and *Michelob* in a blinded fashion. Half of the drinkers preferred *Schlitz*. Apparently, half of the drinkers of the best-selling beer of that era preferred the taste of a less expensive alternative. In reality, these beers were so similar the "taste test" was a set up. There was no control group. Just as likely, half of the beer drinkers who preferred *Schlitz* would have picked *Michelob*, a more expensive beer.

Interpatient variations in response may occur, but we should rely on evidence to guide therapy. Pharmacogenetic reasons could explain these observations, but they must be identified. Comparative effectiveness research is needed to guide therapy.

Patients' responses to pain medications may vary over time. A patient who fails an NSAID could be switched to another drug, and it may work "better." Trying a more expensive brand name NSAID after the failure of a generic might suggest the brand name drug is better, but trying the same inexpensive generic might work just as well.

References available upon request from the Editor.