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B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met January 15, 2013. 1 drug was added in the *Formulary* and 5 drugs were deleted, and 9 drugs were designated nonformulary and not available. 2 drugs were designated high-priority nonformulary drugs, while 1 drug was added in the *Chemotherapy Policy*.

◆ ADDED

Camphorated Opium Tincture (Paregoric®)

◆ DELETED

Asparaginase, *E. Coli* derived (Elspar®)*

**When supplies are depleted; Nonformulary and Not Available*

Codeine*

**All codeine-containing products; Nonformulary and Not Available*

Carbachol Ophthalmic Solution (Isopto Carbachol®)*

**Nonformulary and Not Available*

Homatropine Ophthalmic Solution (Generic)*

**Nonformulary and Not Available*

Nystatin Vaginal Tablets (Generic)*

**Nonformulary and Not Available*

◆ NONFORMULARY AND NOT AVAILABLE

Linaclotide (Linzess®)†

†*Patients may use their own supply*

Methylphenidate Extended-Release Suspension (Quillivant® XR)

Sodium Picosulfate (Prepopik®)

Teriparatide (Forteo®)

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PRESCRIBING

Drug dosing in renal impairment

Why do pharmacists call about the renal dosing of a drug when the estimated glomerular filtration rate (eGFR) in EPIC appears appropriate? Pharmacists usually assess renal drug dosing using the creatinine clearance (CrCL) derived from the Cockcroft-Gault (C-G) equation instead of the estimated glomerular filtration rate (eGFR) derived from the modification of diet in renal disease (MDRD) equation.

GFR is the rate filtrate is formed by nephrons and reflects renal function. Assessing GFR is key when determining a dosage that maximizes the pharmacologic effect and minimizes risks. GFR is most accurately determined by measuring inulin clearance, because it is completely cleared by glomerular filtration. However, this method is impractical and too complex for usual patient care.

Equations have been devised to estimate renal function using a common measurement—serum creatinine (SCr). Creatinine is a byproduct of creatine metabolism that is produced at a constant rate. Most creatinine is filtered by the glomeruli. Using SCr to estimate renal function has limitations. In patients with poor renal function, using CrCL overestimates GFR due to active secretion of creatinine in the renal tubules.

Patient characteristics (nutritional status, muscle mass, and liver function) can affect creatinine formation. Drugs like cotrimoxazole, angiotensin converting enzyme (ACE) inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDs), and cimetidine can increase SCr transiently. Despite these limitations, SCr remains the most common laboratory value to estimate renal function in patients with stable values.[1-3]

For decades, the C-G equation has been the standard for estimating CrCL. First proposed in 1976, the equation was derived by correlating the SCr from 249 adult men with 24-hour urine creatinine collections.[2] Compared to other equations and nomograms at the time, this equation was the most accurate predictor of CrCL. It has been validated in a number of studies.

Like any estimate, the C-G equation has limitations. Controversy exists regarding the most appropriate weight to use to calculate CrCL. EPIC calculates CrCL using actual or ideal bodyweight (IBW), whichever is lower, for normal or underweight patients.[3] For patients greater than or equal to 120% of IBW, EPIC calculates CrCL using an adjusted bodyweight. EPIC is configured to round to 1 mg/dL, if the measured value is less than 1 mg/dL to account for decreased muscle mass. Whether SCr should be rounded up to 1 mg/dL in patients 65 years of age and older is questionable.[4]

The MDRD equation has gained popularity in clinical practice. The equation was developed in 1999 using data collected from 1628 patients with chronic kidney disease.[5]

Because SCr is a variable in the MDRD equation, it has limitations similar to the C-G equation. It is superior to the C-G equation for estimating GFR, and it is the standard for detecting and monitoring chronic kidney disease.[6] Whether the MDRD equation should be routinely used to renally dose medications in controversial. The National Institute of Diabetes and Digestive and Kidney Disease recommends either the MDRD equation or C-G equation for drug dosing.[7]

The C-G equation has been used by drug manufacturers to establish the relationship between drug elimination and kidney function. Almost all renal dosing recommendations are provided in terms of CrCL. Therefore, using the MDRD-derived eGFR to dose drugs is inconsistent with the labeling. Retro-

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◆ **HIGH-PRIORITY NONFORMULARY DRUGS**

Mechlorethamine Injection (Mustargen®)

Teriflunomide (Aubagio®)‡

‡*Restricted distribution program; patients must use their own supply*

◆ **CRITERIA-FOR-USE CHANGES**

Cabozantinib (Cometriq)§

§*Added in the Chemotherapy Policy; Nonformulary Drug*

Camphorated opium tincture [Paregoric®] is an oral alcoholic solution containing morphine (as opium) used for the treatment of non-infectious diarrhea. In November 2011, Paregoric® was deleted from the *Formulary* and designated nonformulary and not available because of "manufacturing problems."

Paregoric® has been re-introduced to the market by Hi-Tech. The Division of Gastroenterology supported the re-addition of Paregoric® in the *Formulary* and the P&T re-added it in the *Formulary*.

Camphorated opium tincture should not be confused with opium tincture. Only a small number of patients need opium tincture.

Opium tincture is dispensed only after the approval of a pharmacy administrator. The pharmacy administrator on-call, working collaboratively with pharmacists, verifies the intended product from the prescriber. The following questions are used since this product could be dangerous to the patient if the wrong drug is selected. *Are you sure you want tincture of opium instead of Paregoric®? Do you know that tincture of opium contains 25 times the opium content as Paregoric®? Has the patient failed Paregoric®?*

***E. coli*-derived asparaginase** has been marketed in the US since 1978 with a labeled indication for the treatment of acute lymphocytic leukemia (ALL) in combination with other agents.

Asparaginase hydrolyzes asparagine and prevents its use in malignant cells, interrupting protein synthesis. Asparagine is an amino acid synthesized by normal tissues and is used in protein synthesis. Some malignant tissues rely on passive diffusion of asparagine into cells for protein synthesis.

For decades, an *Erwinia* asparaginase has been available under an investigational use protocol for patients who cannot tolerate the *E. coli*-derived product. In November 2011, *Erwinia* asparaginase was marketed in the US for patients who have a hypersensitivity to the *E. coli*-derived product. Because the *Erwinia* asparaginase product is so expensive, it was designated a high-priority drug in January 2012. It is only acquired when a patient cannot tolerate the *E.-coli* product. This position was based on its cost (ie, approximately $15,000 per dose).

Unfortunately, *E.-coli* asparaginase is being removed from the market and will be removed from the *Formulary* once supplies have been exhausted. Either the *Erwinia* asparaginase or pegaspargase will have to be substituted. If *Erwinia* asparaginase is always substituted, it would result in approximately a $1.4 million increase in pharmaceutical expenditures at Shands UF.

Children's Oncology Group (COG) protocols may mandate that *Erwinia* asparaginase be used, and there is no flexibility in this requirement. Many adult patients can be switched to pegaspargase, but this will also increase expenditures, if doses are given in the inpatient setting.

Codeine is an opiate used primarily for its analgesic and antitussive properties. It is an alkaloid present in opium. It is perceived as a weak opioid.

Codeine is a prodrug that must be converted to morphine to be pharmacologically active. Codeine is "activated" by the CYP2D6 metabolic system in the liver.

After an FDA alert about the risks associated with CYP2D6 hypermetabolism and overdoses in children (ie, too much morphine leading to respiratory depression and death), particularly children who have undergone tonsillectomies, the Personalized Medicine Program Subcommittee explored the possibility of using CYP2D6 genotyping to help guide therapy.

After discussing this issue with ENT physicians, it was decided to use alternatives to treat pain in this setting. When other alternative pain medications were considered by other frequent prescribers of codeine, genotyping of CYP2D6 was not considered further.

The Medication Safety Subcommittee recommended that codeine be deleted from all order sets, which the P&T Committee passed in November 2012. A newsletter article was published proposing the deletion of codeine from the *Formulary* as a further [more effective] safety measure. This recommendation was made in the context that CYP2D6 monitoring would not be readily available.

When the information on CYP2D6 and codeine was presented at Pediatrics Grand Rounds, some pediatric attending physicians expressed concern about losing codeine as a pain treatment option. They support a proposal to restrict the use of codeine to only patients who are the "right" genotypes (ie, have been genotyped and who are not poor metabolizers [do not adequately form morphine] or ultrarapid metabolizers [form too much morphine]).

The Formulary Subcommittee agreed that the restriction of codeine would be ideal (allow continued safe access of codeine); however, the subcommittee recognized that we currently do not have the ability to operationalize this proposal using EPIC. Since the Personalized Medicine Program's purpose is to develop methods to use pharmacogenetic information clinically, this issue was referred back to the Personalized Medicine Program Subcommittee to work on these operational issues.

Until these operational issues can be established, codeine and all codeine-containing products are no longer listed in the *Formulary*.

Carbachol is a direct-acting parasympathomimetic agent used as an alternative to acetylcholine for miosis. The manufacturer discontinued carbachol ophthalmic drops; therefore, it was deleted from the *Formulary* and designated nonformulary and not available.

Homatropine is a mydriatic agent used for uveal tract inflammation, pre- and post-operative mydriasis, and refraction of the eye. It is generally considered inferior to atropine and cyclopentolate ophthalmic drops. The manufacturer discontinued homatropine ophthalmic drops; therefore, it was deleted from the *Formulary* and designated nonformulary and not available.

Nystatin is a topical antifungal agent used to treat vaginal candida infections. Clotrimazole, fluconazole, and ketoconazole are possible alternatives. The manufacturer has discontinued nystatin **vaginal tablets**; therefore, it was deleted from the *Formulary* and designated nonformulary and not available.

Linaclotide is a guanylate cyclase-C agonist with a labeled indication for the treatment of adults with irritable bowel syndrome with constipation and for chronic idiopathic constipation. Both linaclotide and its active metabolite bind to GC-C and act locally on the luminal surface on the intestinal epithelium. Its actions results in increased intestinal fluid and accelerated gastrointestinal transit.

Linaclotide is given at a dose of 145 mcg for chronic constipation and a dose of 290 mcg for irritable bowel syndrome with constipation. Doses are given once daily on an empty stomach, at least 30 minutes prior to the first meal of the day. Linaclotide is minimally absorbed with low systemic availability following oral administrations. It is contraindicated in pediatric patients up to 6 years of age and in patients with known or suspected mechanical gastrointestinal obstruction.

Efficacy data of linaclotide are based on placebo-controlled studies in patients that met the modified

(continued on next page)

Formulary update, *from page 2*

Rome II criteria. It was shown to be superior to placebo for increasing weekly bowel movements and decreasing abdominal pain. Most trials utilized a 12-week treatment period and approximately one-third of patients responded to treatment. There have been no head-to-head trials comparing linaclotide to current therapies for both chronic and irritable bowel syndrome with constipation.

As expected, diarrhea is the most common adverse reaction reported with linaclotide. Its long-term safety remains unknown. No drug-drug interaction studies have been conducted with linaclotide. Due to its low absorption, no systemic drug-drug interactions or drug interactions mediated by plasma protein binding are anticipated.

Linaclotide costs nearly $7 a day. It was designated as nonformulary and not available, similar to lubiprostone [Amitiza®], which was designated nonformulary and not available in 2007. Patients may use their own supply of linaclotide from home.

Quillivant® XR is an extended-release suspension of the stimulant methylphenidate. It has a labeled indication for the treatment of attention-deficit hyperactivity disorder (ADHD). It is promoted as an option for patients with ADHD who have trouble swallowing tablets and capsules. Currently, pediatricians at Shands UF do not see a niche for the inpatient use of this product.

Quillivant® XR was designated nonformulary and not available. It is a Schedule II (CII) controlled substance, and patients may not use their own supply from home. Immediate-release methylphenidate tablets would be the most likely alternative listed in the *Formulary*.

There are multiple stimulants listed in the *Formulary* including immediate-release methylphenidate and extended-release methylphenidate (ie, Concerta® and Metadate®). Dexmethylphenidate extended-release (Focalin® XR) is also available. Amphetamines are also available (ie, dextroamphetamine, lisdexamphetamine [Vyvanse®], and Adderall®). The stimulants listed in the *Formulary* are driven by the most common drugs that patients are admitted to Shands UF already taking.

Prepopik® has a labeled indication for cleansing the colon in preparation for colonoscopy in adults. It is a combination of **sodium picolfulfate**, a stimulate laxative, and magnesium oxide and anhydrous citric acid, which form magnesium citrate, an osmotic laxative.

Prepopik® is supplied as a powder and must be reconstituted immediately prior to its use. The split-dose method is the preferred dosage. The first dose is given the evening before the colonoscopy. The powder is dissolved in 5 ounces of cold water. It is then followed by five 8-ounce drinks of clear fluids within 5 hours. The second dose is taken the next day during the morning before the colonoscopy. It is followed by at least three 8-ounce drinks of clear fluids within 5 hours and up until 2 hours before the procedure.

The day-before method gives both doses the day before the procedure (ie, the first dose between 4:00 to 6:00 PM and second dose between 10:00 PM to 12:00 AM). Like the first-dose method, the patient follows each dose with five and three 8-ounce clear fluid drinks, respectively.

Patients only drink 10 ounces of diluted drug, and 64 ounces of clear fluids. It is perceived that only drinking 10 ounces of drug will be better accepted by patients.

The Prepopik® container is much smaller than the 4-liter containers of GoLytely® (polyethylene glycol [PEG] 3350 with electrolytes), which would be better for storage. For this reason, Prepopik® was reviewed proactively as a possible replacement for GoLytely®.

Although data suggest Prepopik® is equally efficacious and as well tolerated as other colonoscopy preparations, its most notable disadvantage is its increased acquisition cost (11 times more expensive than GoLytely®), which could add approximately $60,000 to pharmaceutical expenditures. However, improvements in storage and distribution and patient acceptance could justify its increased cost. Another disadvantage is there are no data supporting the use of this product in pediatric patients. Further, Prepopik® is contraindicated in patients with creatinine clearances less than 30 mL/min, which could result in the accumulation of magnesium.

The need to stock 2 products, the lack of acceptance by pediatric gastroenterologists, a concern about proper administration and documentation of the follow-up clear fluids, and the contraindication in patients with impaired renal function led to Prepopik® being designated nonformulary and not available for inpatient use. It is anticipated that outpatient use will occur.

Teriparatide is a recombinant amino terminal fragment of parathyroid hormone (PTH) with a labeled indication for the treatment of osteoporosis. It is the first 34 amino acids of PTH, which produces most of its biological effects.

Teriparatide is indicated at a daily dose of 20 mcg injected subcutaneously for the treatment of postmenopausal women with osteoporosis at high risk of fracture, men and women with glucocorticoid-induced osteoporosis at high risk of fracture, and an increase in bone mass in men with primary or hypogonadal osteoporosis at a high risk of fracture. Teriparatide is available as a multi-dose prefilled pen containing twenty-eight 20-mcg doses.

Clinical trials have shown teriparatide reduces the risk of vertebral and nonvertebral fractures over placebo when used for osteoporosis. However, its relative efficacy in comparison to other therapeutic options for fracture reduction in the treatment of osteoporosis has not been assessed by head-to-head comparison trials. Increases in bone mineral density (BMD), a surrogate outcome for fracture prevention, tend to be higher with use of teriparatide. Yet, the clinical relevance of these increases in BMD is questionable; there is no consensus on the minimal clinically significant difference (MCID) in BMD. Moreover, teriparatide effects are not immediate. It may take up to 28 days after teriparatide initiation for bone formation markers to increase in the serum.

Adverse effects commonly seen with teriparatide include injection site reactions and transient increases in serum calcium. A rare but serious adverse event is osteocarcinoma. Therefore, teriparatide should not be prescribed in those with Paget's disease, unexplained elevations of alkaline phosphatase, open epiphyses, or prior external beam or implant radiation involving the skeleton.

There has been periodic nonformulary use of teriparatide, particularly after bisphosphonates were associated with atypical bone fractures. Some patients were switched to this agent if they had received bisphosphonates for 3 to 5 years for osteoporosis. Inpatient use of teriparatide for the treatment of osteoporosis is deemed unnecessary and is difficult to justify because each pen costs over $1000.

Teriparatide has also been used off-label for bone healing. This use is based on limited data (eg, case reports) and, if effective, is based on long-term therapy. Suspending treatment during a hospitalization is not a problem. The high cost of teriparatide is problematic with fixed reimbursement schemes.

Therefore, teriparatide was designated nonformulary and not available for inpatient use. Since it is an injectable drug, patients may not use their own supply from home.

Mechlorethamine, also known as nitrogen mustard, is a cytotoxic chemotherapeutic that is one of the oldest known "chemo" drugs. Today, it is rarely used to treat cancer; it is sometimes used to treat mycosis fungoides.

Even though it is a very old drug, it is expensive. Mustargen®, marketed by Lundbeck, used to be inexpensive. However, like other rarely used,

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Formulary update, *from page 3*
but necessary, drugs, it is now very expensive…since it is rarely used. Small companies obtain the right to market these rarely used drugs and increase their prices dramatically.

Mustargen® is available for next day delivery from our wholesaler. Thus, it was designation as a high-priority nonformulary agent and will only be obtained for inpatient use when it is absolutely needed.

Teriflunomide is an oral immunomodulator taken twice a day for the labeled indication, the treatment of patients with relapsing forms of multiple sclerosis (MS). It is the second oral drug for this indication; fingolimod (Gilenya®) is also not listed in the *Formulary*.

Teriflunomide is the active metabolite of leflunomide, a drug used to treat rheumatoid arthritis. Leflunomide is listed in the *Formulary*. Teriflunomide works by inhibiting the *de novo* production of pyrimidine nucleotides, thereby reducing T- and B-cell activation, proliferation, and function.

Teriflunomide has demonstrated efficacy in reducing the annualized relapse rate by approximately 30% when compared to placebo in MS patients over a 2-year period. However, no trials have been published to provide direct comparisons to standard MS therapies such as interferon beta or glatiramer acetate. There is one clinical trial in progress comparing the effectiveness and safety of teriflunomide to interferon beta in patients with relapsing MS. Teriflunomide is being investigated as an adjunctive therapy to interferon beta and glatiramer.

The most common adverse effects associated with teriflunomide treatment were mild infections (nasopharyngitis, upper respiratory tract infections, and influenza), fatigue, sensory disturbances, and diarrhea. One of the most common serious adverse effects noted in clinical trials was substantial increases in hepatic enzymes (greater than 8-times the upper limit of normal). This adverse effect is also seen in the parent drug, leflunomide, and both agents carry a black box warning for the risk of liver damage and hepatic failure. Furthermore, teriflunomide carries a black box warning for teratogenicity.

Teriflunomide is not currently available for purchase by hospitals and is only available to patients from authorized distributors. Teriflunomide costs approximately $45,000 per year. In comparison, fingolimod costs approximately $55,000 per year. The cost of treatment with interferon beta-1a is approximately $37,000 annually.

Teriflunomide was designated a high-priority nonformulary drug, since the drug is not currently available for purchase by the hospital or the Shands outpatient pharmacy. EPIC entries will be created specifying that, if continued during the patient's hospitalization, patients will have to use their own supply from home.

Cabozantinib is a kinase inhibitor that blocks abnormal kinase proteins involved in the development and growth of medullary cancer cells. Cabozantinib has a labeled indication for the treatment of patients with progressive, metastatic medullary thyroid cancer. It is given orally once a day on an empty stomach.

The safety and effectiveness of cabozantinib were established in a clinical study involving 330 patients with medullary thyroid cancer. Treatment with cabozantinib increased the length of time a patient lived without the cancer progressing (progression-free survival) and, in some patients, reduced the size of tumors (response rate).

Patients who were given cabozantinib lived an average of 11.2 months without tumor growth compared with an average of 4 months in patients receiving placebo. Results also showed that 27% of patients treated with cabozantinib had reductions in tumor size lasting an average of nearly 15 months, while patients who received a placebo saw no reductions. Treatment with cabozantinib did not extend patients' lives.

The prescribing information for cabozantinib includes a black box warning alerting patients and health care professionals that severe and fatal bleeding and perforations and fistulas in the colon.

The most common adverse effects were diarrhea; inflammation or sores of the mouth; redness, pain, or swelling of the digits (hand-foot syndrome); weight loss; loss of appetite; nausea; fatigue; oral pain; graying or loss of hair color; bad taste; new or worsening high blood pressure; abdominal pain and constipation. The most common laboratory abnormalities included increases in liver enzymes, low calcium and phosphorus, decreased white blood cells and platelets.

Cabozantinib was added in the *Chemotherapy Policy*, but remains nonformulary.

NEWS

New drugs in 2012

Thirty-nine drugs were approved by the FDA in 2012, which is the most new drugs approved in over a decade. Table 1 on page 5 lists unique drugs, new dosage forms, and new combinations.

The FDA touts faster approval times and attribute user fees that manufacturers pay to help hire staff as factor for the increase. Whether this reverses the trend of fewer new drug approvals is unknown, but it does continue several other trends.

Many approvals in 2012 were for drugs that will be used for few patients (ie, orphan drugs). Orphan drugs have a small target population and few patients must be studied in clinical trials. Because few patients will receive these drugs, the cost per year for each patient can be extremely high. For example, Soliris® (eculizumab), which was approved in 2007 for paroxysmal nocturnal hemoglobinuria, is expected to generate $1.5 billion in revenues in 2012 despite being used in few patients.[1] In 2011, it was estimated that orphan drugs accounted for about $50 billion in drug sales, which is about 6% of all drug sales.[1]

Eighteen "biopharmaceuticals" were approved.[2] This trend should continue, since approximately half of drugs in the development pipeline are biopharmaceuticals. It has been difficult for "generic" biopharmaceuticals (biosimilars) to be approved by the FDA. No biosimilars were approved in 2012, but Neutroval® (tbo-filgrastim) is approved in Europe as a biosimilar. Neutroval® went through the complete approval process because the FDA's guidelines for biosimilars took time to establish. One biopharmaceutical approved last year is predicted to have blockbuster potential (ie, sales of $1 billion of more).

Sixteen drugs for cancer patients were approved. Manufacturers seek approval of cancer drugs, because they are often covered by third-party payers. New drugs are anticipated for various types of cancer, cancer diagnosis, or treatment of cancer-related complications.[3]

The P&T Committee proactively reviews new drugs. If a drug fulfills an important niche, it is reviewed proactively and added in the *Formulary* (eg, black widow antivenin, ivermectin, Viokace®, and tenofovir powder). Conversely, some drugs are reviewed and deemed to be not needed for inpatient use at Shands UF (eg, Binosto®, Bydureon®, ingenol mebutate, Korlym®, linaclotide, locaserin, MenHibrix®, peginesatide, Qsymia®, Quillivant® XR, Subsys®, taliglucerase, and tazarotene). The nonformulary use of most new drugs is monitored to determine whether any action is needed.

Apixaban was approved near the end of 2012, after a delay. Its use as an anticoagulant for patients with atrial fibrillation (and probably other off-label uses) has led some to speculate that it

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NEW DRUGS, BIOLOGICALS, & SELECTED DOSAGE FORMS APPROVED BY THE FDA IN 2012

GENERIC NAME	TRADE NAME	INDICATION
aclidinium bromide inhalation	Tudorza Pressiar®	COPD
alendronate sodium	Binosto®	Osteoporosis
allogeneic cultured keratinocytes & fibroblasts in bovine collagen†§	Gentuit®	Mucogingival Surgery Aid
antihemophilic factor, recombinant, plasma free	Xyntha®	Hemophilia A
apixaban	Eliquis®	Anticoagulant
axitinib	Inlyta®	Cancer: Renal Cell Carcinoma
azelastine-fluticasone nasal spray	Dymista®	Seasonal Allergic Rhinitis
balsalazide	Giazo®	Ulcerative Colitis
beclomethasone dipropionate	QNASL®	Seasonal/Perennial Allergic Rhinitis
bedaquiline†	Sirturo®	Tuberculosis
black widow spider antivenin*	Not Specified	Antidote: Black Widow Spider Bites
bosutinib†	Bosulif®	Cancer: CML
cabozantinib†	Cometriq®	Cancer: Thyroid
carfilzomib†	Kyprolis®	Cancer: Multiple Myeloma
choline C 11	None®	Cancer, Prostate: PET Imaging
ciclesonide nasal aerosol	Zetonna®	Rhinitis
crofelemer	Fulyzaq®	HIV Diarrhea
cysteamine†	Cystaran®	Cystinosis
dorzolamide;timolol	Cosopt® PF	Glaucoma
elvitegravir, coricistat, emtricitabine, & tenofovir*	Stribild®	HIV
enzalutamide	Xtandi®	Cancer: Prostate
erivedge	Vismodegib®	Cancer: Basal Cell Carcinoma
estradiol transdermal	Minivelle®	Menopause
exenatide synthetic‡	Bydureon®	Type 2 Diabetes
fentanyl sublingual spray‡	Subsys®	Cancer: Breakthrough Pain
fibrin sealant patch§	Evarrest®	Surgical Bleeding
florbetapir F18	Amyvid®	Alzheimer's: PET Imaging
glucarpidase†§	Voraxaze®	Cancer: Methotrexate Toxicity
icosapent ethyl	Vascepa®	Hypertriglyceridemia
immune globulin, intravenous†§	Bivigam®	Immune Deficiency
influenza vaccine*§	Various	Vaccine: Influenza
influenza vaccine§	Flucelvax®	Vaccine: Influenza
influenza vaccine, quadrivalent§	Fluarix Quadrivalent®	Vaccine: Influenza
ingenol mebutate gel‡	Picato®	Actinic Keratosis
isotretinoin	Absorica®	Acne
ivacaftor‡	Kalydeco®	Cystic Fibrosis
ivermectin*	Sklice®	Head Lice
linaclotide‡	Linzess®	Constipation
linagliptin; metformin	Jentadeto®	Type 2 Diabetes
locaserin‡	Belviq®	Obesity
lomitapide†	Juxtapid®	Hypercholesterolemia
loteprednol etabonate gel	Lotemax®	Ocular Inflammation
loxapine inhalational powder	Adasuve®	Agitation: Schizophrenia & Bipolar
lucinactant	Surfaxin®	Respiratory Distress Syndrome (Infants)
meningococcal + haemophilus vaccine‡§	MenHibrix®	Vaccine
methylphenidate ER‡	Quillivant® XR	Attention Deficit Hyperactivity Disorder
mifepristone†‡	Korlym®	Cushing Syndrome: Hyperglycemia
mirabegron ER	Myrbetriq®	Overactive Bladder
ocriplasmin†§	Jetrea®	Vitreomacular Adhesion
omacetaxine mepesuccinate†	Synribo®	Cancer: CML
oxcarbazepine ER	Oxtellar® XR	Seizures
pancrelipase	Pertzye®	Pancreatic Insufficiency
pancrelipase*§	Viokace®	Pancreatitis/Pancreatectomy
pancrelipase§	Ultresa®	Pancreatic Insufficiency
pasireotide†	Signifor®	Cushing Syndrome
peginesatide‡	Omontys®	Anemia: CKD on Dialysis
perampanel	Fycompa®	Seizures
pertuzumab§	Perjeta®	Cancer:Breast
phentermine; topiramate‡	Qsymia®	Obesity
ponatinib†	Iclusig®	Cancer: CML
raxibacumab†§	Abthrax®	Antibiotic: Anthrax
regorafenib	Stivarga®	Cancer: Colon
sitagliptin;metformin	Janumet® XR	Type 2 Diabetes
sodium picosulfate, magnesium oxide, citric acid‡	Prepopik®	Colonoscopy Prep
tafluprost	Zioptan®	Glaucoma
taliglucerase alfa‡†§	Elelyso®	Gaucher Disease [Type 1]
tazarotene‡	Fabior®	Acne
tbo-filgrastim§	Neutroval®	Cancer: Neutropenia
teduglutide†§	Gattex®	Short Bowel Syndrome
tenofovir powder*	Viread®	HIV
teriflunomide	Aubagio®	Multiple Sclerosis
tobramycin inhaled†	Bethkis®	Cystic Fibrosis
tofacitinib	Xeljanz®	Rheumatoid Arthritis
varicella zoster immune globulin†§	Varizig®	Varicella Exposure
vincristine liposomal†	Marquibo®	Cancer: ALL
ziv-aflibercept	Zaltrap®	Cancer: Metastatic Colorectal

**Listed in the Formulary* *‡Nonformulary and not available* *†Orphan drug* *§Biopharmaceutical*

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B · U · L · L · E · T · I · N

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Renal drug dosing, *from page 1*

-spective studies suggest that the MDRD equation overestimates renal function compared to estimated CrCL, which leads to higher drug dosages than intended in the labeling. This may be dangerous, especially when dosing drugs with narrow therapeutic ranges (eg, enoxaparin or dofetilide). The FDA recognized this discrepancy and published a draft guidance on drug dosing in patients with renal impairment.[8] The FDA recommended that drug manufacturers provide information on drug dosing based on both CrCL and eGFR. However, this practice has not been implemented. Pharmacists will continue to use CrCL to verify dosages for drugs eliminated renally until drug manufacturers begin to provide this information or safety issues related to dosing drugs based on eGFR are resolved. Of course, no estimate is perfect, and clinical judgment should always prevail.

by Matthew Logan Wright, PharmD

References available upon request from the Editor.

New drugs in 2012, *from page 4*

will be a blockbuster drug. Tofacitinib is the biopharmaceutical approved last year expected to be a blockbuster for the treatment of rheumatoid arthritis. Adalimumab (Humira®) is anticipated to have the most sales in the US in 2012. This $9-billion-a-year biological is used to treat arthritis [and Crohn's disease].[4]

Specialty drugs (ie, drugs costing more than $600 per month) are expected to account for 8 of the top 10 drugs (in terms of costs) by 2015.[5] These include biopharmaceuticals, cancer drugs, drugs for autoimmune diseases, and anti-infectives for HIV and hepatitis C.

Despite the high cost of some drugs, overall drug costs are increasing less than in the past. This is attributed to the use of generic drugs for many "small" molecules that have gone off patent. Lipitor®, at its peak, accounted for more than $13 billion in sales worldwide. Atorvastatin is now widely available as a generic. Atorvastatin is 1 of 5 billion-dollar generic drugs, but these "expensive" generics still represent a major decrease in overall expenditures.

Third-party payers encourage patients to use generics by requiring much lower copays. Some plans now have no copays for some generics, and some pharmacies offer generics for $4 for a 1-month supply [or less], and $10 for a 3-month supply. Nearly 80% of all outpatient prescriptions are for generics and many predict that by 2015 90% of all prescriptions will be for generic drugs.

Brand name companies are increasingly offering coupons that decrease a patient's copay when they continue to take a brand name after it is available as a generic. This minimizes the financial impact to the patient, but has major impact on the overall cost of pharmaceuticals. The use of these coupons is illegal for government-funded programs, like Medicare Part D, which considered them an illegal kickback. Coupons and lack of acceptance of generics by some prescribers and patients continues to affect overall healthcare costs.

Important drugs that became available as generics this year include Lexapro® (escitalopram), Seroquel® (quetiapine), and Singulair® (montelukast). In 2013, first-time generics are expected for CellCept® (mycophenolate), Cymbalta® (duloxetine), Lidoderm® (lidocaine transdermal), Lunesta® (eszopiclone), Rilutek® (riluzole), Zometa® (zoledronic acid), and Zomig® (zolmitriptan).

The growing arsenal of generics makes it easier to find a less expensive option in many therapeutic categories. After generics have been on the market for several months, the cost to health systems can drop by as much as 70% or more.

References available upon request from the Editor.