Volume 25, Number 2

Shands at the University of Florida

February 2011

Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met January 18, 2011. 3 drugs were added in the *Formulary*, and 2 dosage forms were deleted. 6 products were designated nonformulary and not available. 4 interchanges and 3 restrictions were approved.

◆ ADDED

Dabigatran (Pradaxa® by Boehringer Ingelheim)

Iron Sucrose (Venofer® by American Regent)

Minocycline Oral (Generic) and **IV** (Minocin® by Triax)*

**IV Restricted*

◆ DELETED

Cisplatin Powder (Platinol® Powder)†

†Nonformulary and Not Available

Phenytoin Injection (Generic)

†Nonformulary and Not Available and Interchanged to Fosphenytoin

◆ NONFORMULARY AND NOT AVAILABLE

Baclofen Injection (Gablofen®)‡

‡Lioresal® is just NF, not NFNA

Ferumoxytol (Feraheme®)

Tesamorelin (Egrifta®)

Tolvaptan (Samsca®)

◆ INTERCHANGES

DTaP (Tripedia®) for **Daptacel®** and **Infanrix®**

Fosphenytoin for **Phenytoin Injection§**

§Same dose in Phenytoin Equivalents

Iron Sucrose Injection for **Sodium Ferric Gluconate Complex**

Tdap (Adacel®) for **Boostrix®**

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NEWS

Abandoned prescriptions?

Drugs do not work if patients do not take them. Noncompliance is an impediment to quality patient care. Therefore, identifying reasons patients do not take their prescriptions is important in order to improve adherence to the drugs that have been prescribed.

Shrank and colleagues recently published an interesting study examining why patients with "good" insurance (mostly employer-based insurance) and reasonable incomes (median income greater than $60,000) failed to pick up their prescriptions from their pharmacy. Examining characteristics of this "prescription abandonment" might alert prescribers and pharmacists of predictors of poor compliance.

Overall, only 1 out of every 30 prescriptions was abandoned in this population. However, remember these patients were well-insured and had incomes that should not prohibit copays for most patients. This could be a bigger problem in patients without insurance and/or with lower incomes.

This study showed that drugs for cough, cold, and allergy or asthma had the highest rate of abandonment. The information on asthma medications was disturbing considering the importance of compliance in controlling a patient's condition. Interestingly, opiates and anti-platelet drugs had the lowest rates of abandonment.

Patients with the lowest incomes (as indicated by the median incomes of their zip codes) were more likely to abandon prescriptions. The higher the co-pay (ie, out of pocket costs), the higher rates of abandonment.

There was also a higher rate of abandonment for electronic prescriptions. This may be a harbinger of another problem that will increase in the future. With electronic medical records (EMRs) used for medication reconciliation, prescribers may assume that since an electronic prescription has been "written," that patients are taking that medication…when they may not. It will be important to determine what medications patients are actually taking, not what we think they are taking based on the EMR.

There is also a higher rate of abandonment for first prescriptions compared with refills. Patients who get their first prescription refilled are more likely to pick up additional refills.

New electronic prescriptions for patients between 18 and 34 years of age with high co-pays are most likely to be abandoned. Understanding why patients do not pick up their prescriptions could help improve patient compliance and, hopefully, patient outcomes.

Abandoned drugs also cause problems for the Shands outpatient pharmacies. Each abandoned prescription is twice the work with no associated revenue. When a prescription is filled, it has to be electronically processed, so the third-party payer (eg, insurance company) authorizes payment. When a prescription is not picked up, the label has to be carefully removed, and the drug returned to stock. The prescription has to be re-processed to give the third-party payer their money back.

Third-party payers audit pharmacies to make sure they get their money back when a prescription is not picked up. If a pharmacy cannot show documentation of a written prescription and that the filled prescription was picked-up (eg, your signature when you get your prescription), the pharmacy must reimburse the payer.

Over a 2-3 week period, 114 prescriptions were abandoned at our outpatient pharmacies. Roughly, 10% of these were employee prescriptions, and half of these had co-pays of $10 or less. This reinforces that written prescriptions do not mean compliance, regardless of the cost of the drug.

REFERENCES

1. Shrank WH, Choudhry NK, Fischer MA, et al. The epidemiology of prescriptions abandoned at the pharmacy. Ann Intern Med 2010;153:633-40.

INSIDE THIS ISSUE

Formulary update, *from page 1*

◆ CRITERIA-FOR-USE CHANGES

Eribulin (Halaven®)*

**Nonformulary Drug Restricted to Chemotherapy Order Form*

Fluoroquinolone-Macrolide Combinations*

**Restricted: Stop the quinolone or macrolide.*

Sodium Ferric Gluconate Complex (Ferrlecit®)*

**Restricted to Outpatient Dialysis Center*

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

Unlike warfarin, dabigatran does not require INR laboratory monitoring, does not interact with foods, and is less susceptible to drug-drug interactions. Its ease of use and convenience compared with warfarin make it a possible replacement for anticoagulation in some patients. However, until more is known about the safety of this product, use should be limited to patients who cannot be adequately controlled with warfarin.

Dabigatran etexilate mesylate is a prodrug that is rapidly converted to its active form by serum esterases. It is a specific and reversible direct thrombin inhibitor. By inhibiting thrombin, fibrinogen cannot be converted to fibrin, inhibiting the formation of a clot. Due to its mechanism of action, there is no antidote for dabigatran, which is a disadvantage. Dabigatran has a half-life of 12 to 17 hours, which requires twice-daily dosing—another disadvantage. Dabigatran is not a substrate, inhibitor, or inducer of CYP450.

Dabigatran is available in 150-mg and 75-mg capsules. The dosage indicated for reduction in risk of stroke or systemic embolization is 150 mg twice daily. The dose indicated for patients with a creatinine clearance of 15-30 mL/min is 75 mg twice daily. Dabigatran was not used in patients with a creatinine clearance under 30 mL/min, a criterion for exclusion in the large trial of dabigatran in non-valvular atrial fibrillation (RE-LY); hence, there is a lack of outcome data to support this low-dose regimen. The 110-mg dose in the RE-LY trial was not approved.

The RE-LY trial examined the safety and efficacy of dabigatran in patients with non-valvular atrial fibrillation compared to warfarin. The primary outcome was time to stroke and systemic embolism; the safety outcome was major hemorrhage. It was concluded that dabigatran 150 mg was superior in efficacy and similar in safety, while the 110-mg dose was noninferior in efficacy and superior in safety. Beyond hemorrhage, other adverse events of note are myocardial infarction (MI) and dyspepsia. Dabigatran was associated with a higher risk of MI, but the significance of this is currently unknown. Dyspepsia was seen in a much greater amount of patients on dabigatran and is most likely due to the tartaric acid core of the capsule, which is needed to promote absorption.

The current cost of dabigatran is $5.07 per day, significantly higher than warfarin, which costs approximately $1 a day. The increased drug cost for dabigatran is somewhat offset by the costs of INR tests associated with the use of warfarin. However, it is estimated that dabigatran is about 3 times more expensive than warfarin, even with the laboratory tests included.

Safety remains an issue with dabigatran. The lack of a monitoring parameter, like INR with warfarin, makes it difficult to determine when patients may be over-anticoagulated and are at risk for bleeding. Patients with a creatinine clearance below 30 mL/min are at increased risk. A dosage reduction to 75 mg BID for patients with a creatinine clearance between 15-30 mL/min may avoid problems. Patients who bleed while on dabigatran should be treated with fresh-frozen plasma or blood. The official labeling should be consulted for guidelines on stopping therapy before a surgical procedure.

Iron sucrose is now the primary injectable iron product listed in the *Formulary*. **Sodium ferric gluconate complex** will no longer be used in the inpatient setting and will be automatically interchanged to the closest available dose of iron sucrose based on vial size. Sodium ferric gluconate complex will continue to be used in the outpatient dialysis unit, since iron sucrose would too expensive in this setting.

All of the currently marketed parenteral iron products, including iron dextran, sodium ferric gluconate complex, iron sucrose, and ferumoxytol, are effective at providing iron supplementation. The decision regarding which products to use is driven by safety, economics, and convenience.

Ferumoxytol is a super paramagnetic iron oxide. Ferumoxytol has a labeled indication for the treatment of iron deficiency anemia in adult patients with chronic kidney disease. The patients who receive this treatment may or may not be receiving hemodialysis at the same time. Ferumoxytol was evaluated as a possible alternative to iron dextran, which is the only parenteral iron product that can be given as a total dose infusion (TDI) of iron.

Due to its individual physiochemical properties, ferumoxytol has less free iron *in vitro* than the other intravenous iron preparations available for the treatment of anemia in chronic kidney disease. The release of free iron into the extracellular space of a cell is associated with many adverse effects seen with other intravenous iron therapies. Due to its unique properties, ferumoxytol may avoid unwanted adverse effects, and it is suggested that those that do occur are not as severe. This has not been validated in head-to-head studies.

In 3 ferumoxytol clinical trials, 2 doses of 510 mg were administered as an IV injection, given 3 to 8 days apart. The recommended administration rate is up to 30 mg-per-second so each individual dose is administered over 17 seconds. The phase III open-label randomized clinical trials analyzing the efficacy and safety of ferumoxytol used oral iron as a comparison. The greatest increase in the mean hemoglobin at day 35 was seen with ferumoxytol in comparison to the oral iron.

Ferumoxytol was well-tolerated in clinical trials. The main adverse effects experienced were diarrhea, nausea, hypotension, constipation, peripheral edema, and dizziness. Fewer patients experienced adverse events while taking ferumoxytol in comparison to oral iron. Ferumoxytol did have higher incidences of hypotension and dizziness. Nevertheless, there was a lower incidence of gastrointestinal adverse effects when compared to oral iron. As with most IV iron preparations, serious hypersensitivity reactions may be experienced with ferumoxytol administration (eg, anaphylaxis). This is why it is important for patients to be monitored closely for signs and symptoms of hypersensitivity for at least 30 minutes after administration, as described in the clinical trials.

Ferumoxytol costs more than twice the cost of the most commonly used IV iron preparation currently used inpatient at Shands per equivalent iron dose. The potential increase in pharmaceutical expenditures led to ferumoxytol being designated nonformulary and not available for inpatient use. It remains available as a 2-dose option in the outpatient setting.

Iron sucrose may have advantages over sodium ferric gluconate complex and ferumoxytol in that it can be diluted in saline and infused over a short period (ie, 15 minutes for a

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Formulary update, *from page 2*
100-mg dose). There have been anecdotal reports of patients not tolerating Ferrlicit® but tolerating iron sucrose. Further, there is published information on off-labeled doses of as high as 500 mg of iron sucrose being given at one time [diluted in 250 mL normal saline and given over 4 hours]. Giving two, 500-mg doses of iron sucrose could be used instead of ferumoxytol. The labeled iron sucrose dose is 100 mg given over 10 doses for a total dose of 1 gram.

Since sodium ferric gluconate complex will no longer be available for inpatient use after February 1, 2011, the P&T Committee approved an automatic interchange to iron sucrose. Typical adult doses of sodium ferric gluconate complex 125 mg IV will be changed to iron sucrose 100 mg IV. If 8 doses are ordered, the duration will be changed to 10 doses (ie, same total amount of iron). For children, sodium ferric gluconate complex doses of 1.5 mg/kg to a maximum dose of 125 mg will be changed to iron sucrose 1 mg/kg to a maximum of 100 mg per dose.

Oral and **IV minocycline** were added in the *Formulary*. IV minocycline will be restricted to approval by Infectious Diseases or the Antimicrobial Management Program.

Minocycline was reviewed for possible addition in the *Formulary* due to the 2009 re-release of the injectable formulation and nonformulary use of the oral product.

Minocycline is a tetracycline derivative originally introduced in 1972. The IV formulation was voluntarily withdrawn from the US market in 2005 and reintroduced in 2009 at the request of the US military. Minocycline, like other tetracyclines, is thought to exert bacteriostatic activity against a broad range of gram-positive and gram-negative organisms through inhibition of protein synthesis. Recently the IV formulation has been described in the treatment of infections due to resistant *Acinetobacter baumannii* and methicillin-resistant *Staphylococcus aureus* (MRSA).

The oral bioavailability of minocycline is 95-100% and food does not appear to affect absorption. Thus, there is no dosing adjustment when changing from IV to oral administration. The recommended dosing scheme for minocycline is a 200-mg loading dose followed by 100 mg every 12 hours. The maximum daily dose should not exceed 400 mg. Pediatric dosing for children above 8 years of age is 4 mg/kg load followed by 2 mg/kg every 12 hours.

Minocycline is widely distributed in the tissues and generally achieves higher concentrations in tissue than serum, although sputum-to-serum ratios in bronchitis patients are 0.6:1. Penetration into the CNS is poor.

Minocycline is generally well-tolerated. The most common adverse effects are gastrointestinal (nausea, vomiting), CNS effects (dizziness, vertigo, lightheadedness, tinnitus), skin discoloration, and photosensitivity. Serious adverse effects generally occur with long-term oral therapy or high doses. These include autoimmune hepatitis, vasculitis, and lupus-like syndrome. A report published in 2005 concluded that minocycline may cause more and different adverse events than doxycycline, although other studies contradict this.

Tetracycline resistance is primarily mediated through the acquisition of genes that code for efflux pumps and ribosomal protective mechanisms. The resistance mechanisms have variable effects on the different tetracycline molecules. Therefore, minocycline may retain activity when doxycycline is inactive. Minocycline may be inactive when tigecycline is active.

The acquisition cost per day for minocycline IV is twice that of doxycycline, yet slightly less than tigecycline. Compared to other selected therapies for MRSA (linezolid or daptomycin), the cost is much less. Compared to other therapies for resistant *A. baumannii*, the cost is moderately higher. Published clinical trials are lacking to compare minocycline to non-tetracyclines.

Use of tigecycline and doxycycline at Shands at UF has been low. It is anticipated that use of minocycline would be limited to niche situations. Using this agent for certain MRSA infections may decrease pressure, preserve activity for other agents, and provide cost benefit to the institution as well. Minocycline may also be a less expensive alternative to tigecycline or other antibiotics for infections caused by susceptible Stenotrophomonas, Enterococcus, or ESBL producing organisms. Additional sensitivity testing (E test) may be required for gram-negative infections. The new Staph microbiology panel will list sensitivities to minocycline. Sensitivities to minocycline and tigecycline do not always correlate.

Because oral minocycline can cause esophagitis when not administered correctly (ie, with enough fluid and with the patient sitting up or the bed elevated), appropriate administration instructions should be considered.

Cisplatin powder is no longer provided for patients undergoing transhepatic arterial chemoembolization (TACE) for the treatment of hepatocellular cancers. Cisplatin is an alkylating agent that is available in an injectable form and used for various types of cancer (eg, testicular cancer). The powder is no longer being manufactured. Bristol-Myers Squibb used to provide this product through the Platinol® Powder Restricted Access Program. The powder has never been approved by the FDA for this indication. Carboplatin may be substituted.

Intravenous phenytoin was deleted from the *Formulary* and was designated nonformulary and not available in August 2008. After that decision, orders were automatically changed to **fosphenytoin,** a water-soluble prodrug of phenytoin with some advantages over parenteral phenytoin (eg, less irritating to veins and can be administered more rapidly).

A shortage of fosphenytoin required the re-addition of IV phenytoin in the *Formulary*, and, temporarily (during the shortage), fosphenytoin orders were automatically interchanged to phenytoin. The fosphenytoin shortage has been resolved; therefore, interchange to fosphenytoin will be done using the same "Phenytoin Equivalent (PE)" doses.

Gablofen® does not differ much from the other currently available intrathecal baclofen formulations, but its manufacturer claims its ease of administration for refills as the primary advantage over competitors. Gablofen® was recently approved for the treatment of severe spasticity; however, intrathecal baclofen was first approved in 1992 as an orphan drug and is now considered a standard of care for the treatment of severe spasticity (eg, associated with spinal cord injury).

Gablofen® is compatible with Medtronic's SynchroMed® II, a programmable drug pump. It does not differ from the currently available baclofen injection, Lioresal® Intrathecal, which is exclusively marketed by Medtronic and manufactured by Novartis. When the pumps are implanted, Lioresal® comes with the pump, so Gablofen® is used only for refills.

Gablofen® comes in ready-to-use vials for ease of administration as well as pre-filled syringes, which may reduce both refill preparation time.

Tesamorelin is a growth hormone releasing factor (GHRF) analog with a labeled indication for the reduction of excess abdominal fat in HIV-infected patients with lipodystrophy. Long-term cardiovascular benefit and safety have not been studied. It is not indicated for weight-loss management and has a weight-neutral effect. There are no data to support improved compliance with antiretroviral therapies in HIV-positive patients taking tesamorelin.

This agent is given once daily as a SQ injection. The onset and offset of action of tesamorelin are not well-described in the literature. However a clinical benefit was not seen until 26 weeks of therapy. Thus, it can be

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Formulary update, *from page 3*
inferred, until data refute this assumption, that missing a few doses of tesamorelin while a patient is hospitalized should not be significant. Therefore, tesamorelin was designated nonformulary and not available for inpatient use.

Tolvaptan is an oral non-peptide selective vasopressin V2-receptor antagonist (VRA) that causes an increase in urine water excretion, resulting in a decrease in urine osmolality and an increase in free water clearance and serum sodium concentrations. It has a labeled indication for the treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium less than 125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure, cirrhosis, and Syndrome of Inappropriate Antidiuretic Hormone (SIADH).

Although tolvaptan has been studied in patients with chronic heart failure, it did not improve all-cause mortality or the combined events of cardiovascular mortality or heart failure morbidity. Hyponatremia studies showed that tolvaptan significantly improved serum sodium to normal levels. However, hyponatremia recurred after discontinuation of tolvaptan but improved once therapy was reinitiated after a week. A peak increase of approximately 6 mEq/L in serum sodium is achieved with tolvaptan. Patients with mild hyponatremia (serum sodium concentration of 130-134 mmol/L) and patients with marked hyponatremia (serum sodium concentration of < 130 mmol/L) had a mean increase in serum sodium levels of 4 mmol/L and 8 mmol/L, respectively, on day 30.

Tolvaptan's most common adverse reactions include thirst, dry mouth, and polyuria/pollakiuria. Tolvaptan contains a black-box warning indicating that too-rapid correction of serum sodium (eg, greater than 12 mEq/L over 24 hrs) may result in osmotic demyelination syndrome. During initiation and titration, close monitoring of serum sodium and volume status is necessary in patients receiving tolvaptan. Tolvaptan is contraindicated in patients who have an urgent need to increase sodium, those who are unable to autoregulate thirst, patients with hypovolemic hyponatremia, patients on concomitant potent CYP3A4 inhibitors, and anuric patients. Tolvaptan can induce copious aquaresis causing dehydration and hypovolemia, especially in volume-depleted patients who may be on diuretics or who are fluid-restricted. Fluid restriction during the first 24 hours of therapy and concomitant use of hypertonic saline should be avoided.

Conivaptan is the only other VRA available in the US; it is administered parenterally and targets the V_{1a} and V_2 receptors. Conivaptan use must be approved for the management of patients with euvolemic and hypervolemic hyponatremia.

Conivaptan differs from tolvaptan in that it must be administered for the full course of treatment in a hospital and may cause hypotension or hypertension. It is, however, doubtful that tolvaptan would be used outside of a hospital setting. Also, tolvaptan has more drug-drug interactions than conivaptan. Both drugs are contraindicated with potent CYP3A inhibitors like ketoconazole, clarithromycin, ritonavir, nelfinavir, saquinavir, nefazodone, and indinavir.

A disadvantage of tolvaptan is cost. Each tolvaptan tablet (either 15 or 30 mg) is $240.87, which is taken every day for an indefinite time until hyponatremia resolves. Off-labeled use is a concern.

Tolvaptan was designated nonformulary and not available. Conivaptan is available to increase serum sodium levels temporarily in the inpatient setting. Use must be approved by a clinical pharmacist. Patients may qualify for conivaptan therapy if they are in an ICU or IMC and have low serum sodium levels that prevent them from going to the operating room for a procedure. All other measures to increase serum sodium must have failed prior to initiation of conivaptan therapy. Due to a high incidence of injection-site reactions, conivaptan can be infused via a peripheral line for a maximum of 12 hours. A central line must be placed after this period for further therapy to be approved.

DTaP is **diphtheria, tetanus, and acellular pertussis vaccine,** which is used routinely in young children. **Tdap** is **tetanus, diphtheria, and acellular pertussis vaccine** and is used as a booster in older children and adults.

According to Centers for Disease Control's (CDC) Advisory Committee on Immunization Practices (ACIP), the same manufacturer of the DTaP and Tdap vaccines should be used for the entire series "whenever feasible;" however, the vaccine should not be deferred if the previously used brand is not available or unknown. Data on the safety and immunogenicity of interchanging vaccines from different manufacturers is limited.

There are three different brands of the DTaP vaccine: **Daptacel**® and **Tripedia**® by Sanofi Pasteur, and **Infanrix**® by GlaxoSmithKline. There are 2 Tdap vaccine brands: **Adacel**® by Sanofi Pasteur, and **Boostrix**® by GlaxoSmithKline. Shands at UF currently carries Tripedia® and Adacel®. DTaP and Tdap vaccines will be interchanged to the brand that is currently available at Shands at UF, regardless of the brand that the patient has previously received per a P&T-approved interchange.

Eribulin is a microtubule inhibitor with a labeled indication for the treatment of patients with metastatic breast cancer who have previously received at least 2 chemotherapy regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.

Eribulin was added in the *Chemotherapy Policy*, [requiring the use of a *Chemotherapy Order Form*], but remains a nonformulary drug. It is anticipated that it will be used mostly in the outpatient setting.

Azithromycin is the primary **macrolide** listed in the *Formulary*. **Ciprofloxacin** and **levofloxacin** are the primary **fluoroquinolones**. After reviewing the evidence regarding the use of fluoroquinolones in combination with macrolides for community-acquired pneumonia (CAP) and Legionnaire's disease, the P&T Committee empowered the Antimicrobial Management Program to discontinue one of these agents when they are being used together to treat a bacterial infection.

The IDSA/ATS pneumonia guidelines and a preponderance of data support monotherapy for the management of Legionnaire's disease. Clinical trials evaluating the efficacy of a fluoroquinolone or macrolide have consistently demonstrated that either regimen results in high cure rates. There are in-vitro data supporting combination macrolide and fluoroquinolone against *L. pneumophila,* but no clinical evidence exists to support this combination therapy. In addition, there is an increased risk for adverse events, including Torsade de pointes.

Based on these data, the Anti-Infective Subcommittee recommended that the combination of fluoroquinolones and macrolides be avoided in patients with CAP and patients suspected of having Legionnaire's disease.

Healthcare providers can continue to prescribe a fluoroquinolone-macrolide combination in the following scenarios with a warning for concerns for adverse events: cystic fibrosis and bronchiolitis obliterans when levofloxacin or ciprofloxacin may be used in combination with azithromycin (ie, azithromycin is being used as an anti-inflammatory agent) and when azithromycin is used for gastrointestinal motility issues in combination with levofloxacin or ciprofloxacin (ie, azithromycin is used as a prokinetic agent).

NEW DRUGS, BIOLOGICALS, & SELECTED DOSAGE FORMS APPROVED BY THE FDA IN 2010

GENERIC NAME	TRADE NAME	INDICATION
Acetaminophen Injection†	Ofirmev®	Pain and Fever
Alcaftadine^	Lastacaft®	Conjunctivitis, Allergic
Alglucosidase alfa^	Lumizyme®	Pompe Disease
Aliskiren-Amlodipine†‡	Tekamlo®	Hypertension
Aliskiren-Amlodipine-Hydrochlorothiazide†	Amturnide®	Hypertension
Alpha-1-protease Inhibitor	Glassia®	Emphysema
Baclofen Injection†‡	Gablofen®	Spasticity
Buprenorphine Transdermal†‡	Butrans®	Chronic Pain
Cabazitaxel^	Jevtana®	Cancer: Prostate
Calcipotriene Foam†‡	Sorilux®	Psoriasis
Carglumic acid^	Carbaglu®	N-acetylglutamate Deficiency
Ceftaroline^	Teflaro®	Antibiotic
Clindamycin-Tretinoin†‡		Acne
Collagenase Clostridium Histolyticum‡	Xiaflex®	Dupuytren's Contracture
Dabigatran^	Pradaxa®	Anticoagulant: Atrial Fibrillation
Dalfampridine^	Ampyra®	Multiple Sclerosis
Denosumab^‡	Prolia®	Osteoporosis
Dextromethorphan-Quinidine†	Nuedexta®	Pseudobulbar Affect
Donepezil†	Aricept®	Alzheimer's Disease
Doxepin†‡	Silenor®	Insomnia
Dutasteride-Tamsulosin†‡	Jalyn®	Benign Prostatic Hypertrophy
Eribulin^	Halaven®	Cancer: Breast
Esomeprazole-Naproxen†‡	Vimovo®	Pain: Arthritis
Ethinyl estradiol, Drospirenone, Levomefolate‡	Beyaz®	Oral Contraceptive
Ethinyl estradiol, Drospirenone, Levomefolate‡	Safyral®	Oral Contraceptive
Ethinyl estradiol, Norethindrone, Ferrous fumarate‡	Lo Loestrin® FE	Oral Contraceptive
Estradiol valerate, Dienogest^‡	Natazia®	Oral Contraceptive
Everolimus^	Zortress®	Transplant Organ Rejection
Fibrin Sealant Patch†	TachoSil®	Cardiovascular Surgery
Fingolimod^	Gilenya®	Multiple Sclerosis
Gatifloxacin Ophth†	Zymaxid®	Conjunctivitis, Bacterial
Glycopyrrolate†‡	Cuvposa®	Drooling
Hexaminolevulinate	Cysview®	Diagnostic: Bladder Cancer
Hydromorphone ER†‡	Exaglo®	Pain
Immune Globulin, SQ†‡	Hizentra®	Primary Immunodeficiency
IncobotulinumtoxinA‡	Xeomin®	Cervical Dystonia & Blepharospasm
Influenza Virus Vaccines	Various	Influenza Prevention
Ketorolac Nasal Spray†‡	Sprix®	Pain
Lamotrigine ER†‡	Lamictal® XR	Seizures
Liraglutide^	Victoza®	Diabetes
Lurasidone^	Latuda®	Schizophrenia
Mannitol†	Aridol®	Asthma Diagnostic
Memantine ER†‡	Namenda® XR	Alzheimer's Disease
Meningococcal Vaccine‡	Menveo	Prevention of Meningococcal Infection
Mometasone-Formoterol†	Dulera®	Asthma
Moxifloxacin Ophth†	Moxeza®	Conjunctivitis, Bacterial
Olmesartan-Amlodipine-Hydrochlorothiazide†‡	Tribenzor®	Hypertension
Ondansetron Film†‡	Zuplenz®	Nausea and Vomiting
Paliperidone Palmitate†‡	Invega® Sustenna	Schizophrenia
Pancrelipase*	Pancreaze®	Pancreatic Insufficiency
Pegloticase^‡	Krystexxa®	Gout
Pneumococcal Vaccine*	Prevnar-13®	Prevention of Pneumococcal Infections
Polidocanol^	Asclera®	Spider Veins
Pramipexole ER†‡	Mirapex® ER	Parkinson's Disease
Risedronate†‡	Atelvia®	Osteoporosis
Ritonavir Tablet*†	Norvir®	HIV
Saxagliptin-Metformin†	Kombiglyze® XR	Diabetes
Sipuleucel-T^‡	Provenge®	Cancer: Prostate
Sodium & Potassium sulfate – Magnesium Citrate†	Suprep®	Laxative: Bowel Prep
Tesamorelin^‡	Egrifta®	HIV Lipodystrophy
Testosterone, Topical†‡	Axiron®	Hypogonadism
Testosterone, Topical†‡	Fortesta®	Hypogonadism
Toclizumab^	Actemra®	Rheumatoid Arthritis
Trazodone ER†‡	Oleptro®	Depression
Triptorelin Pamoate‡	Trelstar®	Cancer: Prostate
Ulipristal acetate^	Ella®	Oral Contraceptive, Emergency
Vardenafil†‡	Staxyn®	Erectile Dysfunction
Velaglucerase alfa^‡	Vpriv®	Gaucher Disease

^New Molecular Entities (NMEs)
*Listed in the Formulary
†New Dosage Form, Combination, or Indication
‡Nonformulary and not available

Drugs & Therapy
B · U · L · L · E · T · I · N

Volume 25, No. 2 February 2011
This publication is produced by the Drug Information and Pharmacy Resource Center under the direction of the Department of Pharmacy Services and the Pharmacy and Therapeutics Committee.

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NEWS

New drugs in 2010

There were 21 new unique drugs (ie, New Molecular Entities) approved in 2010 (see table on page 5). This was a decrease compared with 25 last year. The year started out with many new approvals, but the number of new approvals slipped at the end of the year. Several drugs that were reviewed near the end of the year were delayed requiring additional information. There also appeared to be a slight decrease in the number of new biologicals approved. There were many new dosage forms or combinations approved.

The trend of approving boutique drugs also continues. For example, carglumic acid was approved for N-acetylglutamate deficiency, alglucosidase for Pompe disease, and valaglucerase for Gaucer disease.

There were several drugs approved for the treatment or prevention of cancer. Manufacturers seek approval of drugs used for the treatment of cancer, since usually these drugs are covered by third-party payers.

Four new oral contraceptives were approved, 2 with levomefolate.

Three combination antihypertensive agents were approved, continuing the trend of marketing combinations for the treatment of hypertension.

Five new extended-release versions of drugs were approved as the patents expired on the immediate-release dosage forms.

2010 was another big year for first-time generics approvals. Generic versions of blockbuster drugs continue to be marketed as patents expire. Many third-party payers encourage patients to use generics by requiring much lower co-pays. Some plans now have no co-pays for some generics, and Walmart and many other retailers offer many generics for $4 for a 1-month supply, and $10 for 3 months' supply. At least 2/3 of all prescriptions filled are now generic drugs, yet they account for less than 1/4 of all expenses.

Important first-time generic versions of brand name drugs approved in 2010 included generic versions of common drugs used in the ambulatory setting like Ambien CR® (zolpidem ER), Effexor® XR (venlafaxine ER), Strattera® (atomoxetine), Temodar® (temozolomide), and Yasmin®. Other important generics used in health systems include Azactam® (aztreonam), Cosmegen® (dactinomycin), Gemzar® (gemcitabine), Hycamtin® (topotecan), Keppra® IV (levetiracetam), Lovenox® (enoxaparin), Merrem® (meropenem), and Vfend® tablets (voriconazole). New generics expected for 2011 include Lipitor® (atorvastatin), Uroxatral® (alfuzosin), Xalatan® (latanoprost), and Zyprexa® (olanzapine).

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.