

New drug update 2011

INTRODUCTION

Numerous products are developed, studied and ultimately reviewed yearly by the Food and Drug Administration. It is estimated that only 5-out-of-5,000 developed compounds actually receive FDA approval.¹ Throughout 2010 and 2011, a number of products have been approved for patient use. For the busy clinician, it is extremely difficult to keep up with all of the newly approved products, various label changes and new indications for already approved products. Despite this difficulty, it is imperative that clinicians be familiar with new medications, how these medications may be utilized and most importantly, with which products an interaction may occur. This article will provide the clinician with an overview of the various medication approvals from 2010 and 2011, as well as many of the label changes and updates that have occurred.

NEW MEDICATION APPROVALS

Aliskiren

Aliskiren (Tekturna®) is a direct renin inhibitor and the first within this class of antihypertensives to hit the U.S. market. It is available in two strengths, 150 mg and 300 mg, and is believed to work

at the point of activation of the renin-angiotensin-aldosterone system to regulate blood pressure by lowering levels of angiotensin I, angiotensin II and plasma renin activity.² At present, it is indicated for the treatment of adults with hypertension and may be co-administered with other antihypertensive agents, including angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and thiazide diuretics. Clinicians should be cautious when using in patients with moderate to severe renal disease due to the absence of clinical trials and safety information in this population, as well as with maximum dosages of ACE inhibitors due to the risk of hypotension. In addition, patients with diabetes may be more likely to develop hyperkalemia when using aliskiren and should be regularly monitored. It is a pregnancy category C in the first trimester and a pregnancy D in the second and third trimesters, making this product unacceptable for pregnant women. In patients taking cyclosporine or itraconazole, aliskiren is contraindicated. From a side-effect profile, it generally is well-tolerated, with adverse events similar to those with a placebo. The prevalence of diarrhea (2.3%) is the most common adverse

event reported in clinical trials.² Providers should closely monitor the patient for hypotension, particularly when aliskiren is added to other antihypertensives. It is important to note that two cases of angioedema were reported in clinical trials. From a safety perspective, if a patient has had angioedema from an ACE or an ARB, aliskiren also should be avoided.

Denosumab

Denosumab (Prolia™) is a receptor activator of nuclear factor kappaB ligand, or RANKL. It is a human IgG2 monoclonal antibody with affinity and specificity for human RANKL, and is produced in genetically engineered mammalian (Chinese hamster ovary) cells. At present, it is indicated for postmenopausal women with osteoporosis at high risk for fracture.³ Subcutaneously administered by a healthcare professional, it is a 60-mg dosage that is given every six months. It may be administered into the upper arm, upper thigh or abdomen. Like all medications that treat osteoporosis, it is contraindicated in patients with serum hypocalcemia. It is imperative that serum calcium levels be checked prior to the administration of denosumab because it has

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Program Goal: To improve the advanced practice clinician's awareness of and ability to counsel patients regarding newly released medications, including indications, side effects, risks and benefits.

Learning Objectives:

Upon completion of this program, the advanced practice clinician should be able to:

1. Identify 10 to 15 new medications being utilized in the primary care setting.
2. Recall the use and benefits of each of the new medications.
3. Describe the potential side effects and drug-drug interactions of each of the new medications discussed.
4. Explain updates related to labeling, indications and risks associated with various medications.
5. Educate patients on new medications, including benefits and risks.

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been known to exacerbate hypocalcemia.

From an efficacy standpoint, new vertebral fractures occurred in 7.2% of patients randomized to placebo, 2.3% receiving denosumab.³ Hip fractures occurred in 1.2% of patients receiving placebo, 0.7% receiving denosumab. Bone density improved by 8.8% in the lumbar spine, 6.4% in the total hip and 5.2% in the femoral neck. All of these results were obtained from a three-year pivotal clinical trial and were based upon comparison with a placebo.³ Precautions for this medication include the risk for serious infections, which occurred at a rate of 3.3% in the placebo group and 4% in the active treatment arm.³ Three cases of endocarditis were documented in those receiving denosumab, while zero occurred in the placebo group. It is believed that the increased risk of infection may be related to this drug's mechanism of action as a RANKL activator. RANKL is expressed on T and B lymphocytes and in lymph nodes. In addition, patients should be monitored for rashes and skin infections. Like all medications that treat osteoporosis, this new class of medication also carries a warning for osteonecrosis of the jaw. Patients should be cautioned regarding oral surgery, and clinicians should refer all patients needing significant dental work to a dentist or oral surgeon prior to initiating this medication.

One potential advantage for denosumab is that there is no dosage adjustment required for patients with renal impairment or chronic kidney disease. Recently, denosumab, which also is sold as XGEVA[®], received a new indication for the prevention of skeletal-related events in patients with bone metastases from solid tumors (e.g., prostate cancer).⁴ XGEVA[®] will compete with an older product that has been on the U.S. market for years, called zoledronic acid (Zometa[®]).

Dabigatran etexilate mesylate

When it was approved by the FDA, dabigatran etexilate mesylate (Pradaxa[®]) received a lot of publicity due to its potential to ultimately replace warfarin (Coumadin[®]) in the future. At present, dabigatran is only indicated for the reduc-

tion systemic embolism and stroke in patients with nonvalvular atrial fibrillation.⁵ This new anticoagulant works as a direct thrombin inhibitor. For patients who are in need of an anticoagulant and are not yet taking one, dabigatran is dosed in the following manner: 150 mg twice daily (if creatinine clearance > 30 mL/min) and 75 mg twice daily (if creatinine clearance 15 mL/min to 30 mL/min).⁵ In the "Randomized Evaluation of Long-term Anticoagulant Therapy" study, patients with atrial fibrillation who had an increased risk of stroke were randomly assigned to receive dabigatran 110 mg two times daily, 150 mg twice daily or warfarin over a two-year period. In this study, dabigatran showed statistical significance in decreasing hemorrhagic and ischemic strokes when compared with warfarin.⁶ From a safety perspective, the most commonly reported adverse events included bleeding, stomach pain, nausea and heartburn.⁵ Patients should be advised to take dabigatran with food for better tolerability.

Some of the clinical advantages to this medication are the lack of need to monitor the international normalized ratio or other laboratory parameters, the lack of interaction with foods containing vitamin K and the absence of significant drug/drug interactions (except rifampin). However, the cost of this product is significantly higher than that of warfarin, even when the cost of INRs are factored into the economic equation. If the patient currently is taking warfarin and the clinician is switching the patient to dabigatran, the following protocol should be utilized. The clinician should discontinue warfarin and monitor the INR daily until the INR becomes subtherapeutic. For most patients, subtherapeutic generally is defined as an INR of less than 2. Once the INR is subtherapeutic, dabigatran is then initiated.

Dabigatran is documented to be effective within two hours of the first dose. For patients who are hospitalized and need to be converted from a parenteral anticoagulant to dabigatran, dabigatran may be started zero to two hours before the next parenteral dose is due or upon discontinuation of the heparin infusion. Unfortunately, there is no antidote for

this product. Of concern is how to best proceed with the patient needing emergency surgery and how to best minimize the risks of this surgery from a bleeding perspective given the absence of an effective antidote. Clinicians prescribing or managing patients on this medication must continue to watch the literature for clinical updates regarding this scenario. For those requiring a planned surgery, dabigatran must be stopped one day before surgery in those without chronic kidney disease, or three days prior to surgery in anyone with CKD. Patient adherence to the medication must be emphasized because it begins to lose efficacy within 15 hours after the last dose. If a dosage is inadvertently omitted by the patient, the patient should be instructed to take the next dose as soon as possible unless the next dose is due within six hours. Patients should avoid doubling up on the dose.

Liraglutide

Liraglutide (Victoza[®]) belongs to a class of medications called glucagon-like peptide-1, or GLP-1, receptor agonist and joins exenatide (Byetta[®]) in this marketplace. It is indicated for adults with Type 2 diabetes and may be used as monotherapy or added on to other agents for the treatment of this complex condition. It is administered by the patient into the abdomen, thigh or upper arm as a once-daily subcutaneous injection and may be dosed at any time of the day, independent of meals.⁷

When initiating liraglutide, it should be dosed at 0.6 mg once daily for one week. If the patient tolerates this dosing regimen, the dosage may be increased to 1.2 mg for one week, with the ultimate goal of 1.8 mg once daily as needed to achieve glucose and A1C control. The clinician certainly may adjust the patient's dosing if he or she experiences such side effects as nausea or vomiting. When compared with placebo, clinicians can expect a 1.1% decrease in A1C from baseline and a 2.5-kg weight loss.⁷

Precautions include a history of pancreatitis (safety studies have not been conducted), thyroid C-cell carcinomas (medullary thyroid carcinoma), hypoglycemia

and gastroparesis (due to its mechanism of action). It is a category C in pregnancy and is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome due to a dose-dependent and duration-related increase in thyroid tumors in mice and rats during clinical trials. It is unknown whether this effect will be seen in humans, but until such information is clearly delineated, the warning will remain. Most commonly reported side effects are nausea, diarrhea, vomiting, constipation and upper respiratory infections.⁷

Dofetilide

Dofetilide (Tikosyn[®]) is a class III antiarrhythmic medication indicated for the maintenance of normal sinus rhythm in patients with atrial fibrillation/atrial flutter after having been converted to NSR and for the conversion of patients with atrial fibrillation and atrial flutter to NSR.⁸ It is not indicated for patients with paroxysmal atrial fibrillation and should be reserved for those with highly symptomatic atrial fibrillation/flutter due to risks of ventricular arrhythmias. Dofetilide works by blocking the cardiac ion channel carrying the rapid component of the potassium current. It has no effect on sodium channels (Class I effect), adrenergic alpha-receptors or adrenergic beta-receptors. It increases action potential duration in a predictable concentration-dependent manner and delays repolarization.⁸ While it has the potential to prolong the QT interval, it has no effects on the PR or QRS interval. This product only should be initiated within the hospital or inpatient setting so that proper monitoring of the patient may occur.⁸ Prior to initiation, the potassium and the QTc/QT must be normal.

The dosage is determined by the patient's creatinine clearance: > 60 mL/min, 500 mcg two times daily; 40 mL/min to 60 mL/min, 250 mcg two times daily; 20 mL/min to 40 mL/min, 125 mcg two times daily; and < 20 mL/min, it is contraindicated.⁸ Once initiated, the QTc/QT must be rechecked within two to three hours after first dose, and the dosage must be adjusted accordingly. Patients should

be monitored inpatient for a minimum of three days after drug initiation. The achieved dosage is clearly associated with the efficacy of the product in converting the patient from atrial fibrillation/flutter to NSR and maintaining this normal rhythm. The 125-mcg twice-daily dosing schedule is associated with 6% conversion from atrial fibrillation/atrial flutter to NSR in both clinical trials and 32% maintenance of NSR at the 12th month. Conversely, for those receiving the 500-mcg twice-daily dosing, there is a 30% and 29% (two clinical trials) conversion rate, while 46% remain in NSR at 12 months.

Clinicians using this product must be very aware of the numerous contraindications and drug/drug interactions, including prolonged QT syndrome, verapamil, cimetidine, trimethoprim, ketoconazole and hydrochlorothiazide. While this product has been on the market for a few years, there have been numerous updates to its labeling, and as such, clinicians must be made aware of these changes, as well as the product's numerous drug interactions.

Vilazodone

Vilazodone (VIIBRYD[™]) is a new antidepressant to hit the market and is indicated for the treatment of major depressive disorder in adults. It is a selective serotonin reuptake inhibitor, or SSRI; 5-HT_{1A} partial agonist; and is recommended to be initiated at 10 mg once daily. The maximum dosage is 40 mg once daily and is available in three strengths to ease dosage titration: 10 mg, 20 mg and 40 mg.⁹ It should be dosed with food because taking vilazodone on an empty stomach is associated with a decrease in the absorption and possibly efficacy.

Vilazodone is contraindicated in patients who are currently taking or have taken monoamine oxidase inhibitors, MAOIs, within the previous 14 days. It carries the same warnings and precautions as all SSRIs, including the risk of suicidal ideations, serotonin syndrome, seizures, abnormal bleeding — particularly when also using a nonsteroidal anti-inflammatory drug, or NSAID — serotonin withdrawal and pregnancy/lactation. In patients taking strong

CYP3A4 inhibitors, such as ketoconazole, erythromycin and clarithromycin, vilazodone dosing should not exceed 20 mg once daily.⁹ Conversely, for those taking CYP3A4 inducers, the efficacy of vilazodone may be diminished.

Most commonly reported side effects include diarrhea, nausea, dry mouth and dizziness. During the marketing campaign for this product, clinicians will likely hear representatives cite information that vilazodone may be less likely to cause sexual dysfunction. Clinicians are reminded that the number of patients studied to garner this particular marketing strategy is very small, and conclusions should not be drawn from these numbers. Sexual dysfunction was reported in 15-out-of-170 males, compared with one in the placebo group, and 5-out-of-266 women, compared with zero in the placebo group. In terms of weight, the group receiving vilazodone gained 0.16 kg, compared with 0.18 kg in those receiving placebo. Vilazodone is a category C in pregnancy and has been shown in trials to be excreted into the breast milk of lactating rats. As such, this product only should be used in pregnant or lactating women when the benefits clearly outweigh the potential risks.

Prasugrel

Prasugrel (Effient[®]) was approved for the reduction of thrombotic cardiovascular events, including stent thrombosis, in patients with acute coronary syndrome who are to be managed with a potent carboxypeptidase inhibitor as follows: patients with unstable angina, or non-ST-elevation myocardial infarction, and patients with ST-elevation myocardial infarction when managed with either primary or delayed PCI. It joins the class of medications known as P2Y₁₂ platelet inhibitors and is in direct competition to clopidogrel (Plavix[®]). Prasugrel is dosed by administering a 60-mg loading dosage followed by 10 mg once daily unless the patient weighs less than 60 kg. In the patient weighing less than 60 kg, 5 mg once daily is the recommended dosage.¹⁰ It may be co-administered with aspirin, although the risk of bleeding may be

greater. Patients should be advised to take this product with food.

Prasugrel is contraindicated in the patient with active pathological bleeding or a previous history of transient ischemic attacks or cerebrovascular accident. Given its mechanism of action, coumadin and NSAIDs are considered drugs to avoid when using this product due to the increased risk of bleeding. At present, it does not appear to interact with proton-pump inhibitors, which may prove to be a big selling point for this product, particularly when comparing it to the market leader, clopidogrel (Plavix®). Of note, clopidogrel is anticipated to achieve generic status by the end of 2011.

From an efficacy standpoint, studies were conducted comparing prasugrel to clopidogrel. Prasugrel appears to be more efficacious than clopidogrel in reducing myocardial infarctions but is associated with higher rates of bleeding, with the highest risk of bleeding occurring early on in treatment (4.5% vs. 3.4%).^{11,12} Clinicians should be aware that prasugrel may cause fatal bleeding, must be discontinued seven days prior to surgery and should be avoided in individuals older than 75 years of age due to an increased risk of bleeding. Patients must be counseled that adherence to this regimen is key because abruptly or prematurely stopping prasugrel may increase risk of a myocardial infarction.

Miconazole

Miconazole (Oravig®) is a new antifungal agent indicated for oropharyngeal candidiasis in adults. Unlike clotrimazole (Mycelex Troches®), which is administered five times daily, miconazole (Oravig®) is a 50-mg buccal tablet designed to be dissolved in the gum region and is administered once daily to the upper gum region for 14 consecutive days.¹³ Patients should be instructed to avoid chewing, crushing or swallowing this dissolvable tablet. The most common adverse events seen in trials included diarrhea, headache, nausea, vomiting and upper abdominal pain. In patients taking warfarin, INR should be closely monitored given the potential for a drug/drug interaction and the increased risk of pathological bleeding.¹³

Guanfacine

Guanfacine (Intuniv®) is a selective alpha-2A adrenergic receptor agonist approved for the treatment of attention deficit hyperactivity disorder in children and adolescents ages 6 years to 17 years of age. Guanfacine was first approved in 1986 and marketed as an antihypertensive called TENEX®. The mechanism by which guanfacine works for ADHD is not currently known.¹⁴ For the treatment of ADHD, guanfacine should be dosed once daily and may be administered as monotherapy or in combination with stimulants for the treatment of this condition. Patients should be advised to avoid chewing or crushing this extended-release tablet and to avoid taking it with a high-fat meal since both will increase exposure to guanfacine.

Dosing should be initiated at 1 mg per day and increased by 1 mg daily after one week, as needed to control symptomatology.¹⁴ The maximum dosage is 4 mg once daily. Dosages higher than 4 mg once daily have not been studied. Similarly, when guanfacine is discontinued, the dosage should be slowly decreased by 1 mg every three to seven days.¹⁴ Given its mechanism of action, common side effects include low blood pressure, bradycardia, sedation and nausea. Co-administration with ketoconazole and other strong CYP3A4/5 inhibitors may increase the plasma concentration of guanfacine, thus increasing the risk of serious adverse events, such as hypotension, bradycardia and sedation. Co-administration of guanfacine and valproic acid can result in increased concentrations of valproic acid. When guanfacine is co-administered with valproic acid, valproic acid concentrations should be monitored and patients should be counseled regarding the potential for increased side effects.

COMBINATION THERAPY

One of the current trends in pharmacotherapy is the development of combination products. With so many commonly prescribed medications achieving generic status, manufacturers are able to introduce new products to the marketplace without having to develop a novel

compound and conduct lengthy clinical trials.¹⁵ To introduce a combination product with previously tested and approved ingredients, manufacturers are more easily able to demonstrate equal efficacy and safety to ultimately achieve FDA approval, thus making combination products an attractive option.¹⁵

In no other disease state have we seen combination products introduced more frequently than with hypertension. Several new combination products, some of which contain three medications, have been FDA-approved. Examples of newly approved combination products include: Tekamlo™ (aliskiren and amlodipine), Tribenzor™ (olmesartan medoxomil, amlodipine and hydrochlorothiazide) and Amturnide™ (aliskiren, amlodipine and hydrochlorothiazide).^{16,17,18} Combination therapy also is more commonly utilized in individuals with Type 2 diabetes. Over the past year, Kombiglyze™ XR (saxagliptin and metformin ER) has been introduced to the market. This combination of a DPP-4 inhibitor and a biguanide is indicated for Type 2 diabetes and is administered as a once-daily formulation. Once-daily dosing is appropriate for this medication because the metformin found in Kombiglyze® is an extended-release formulation.

The maximum dosage for this product is 5/2,000 mg daily. Clinicians can expect an A1C reduction of 2.5% with maximum dosing (A1C at baseline = 9.4%).¹⁹ Of increasing importance is the emerging evidence that metformin, when administered to patients for prolonged periods of time, may be associated with an increased risk of a B12 deficiency.¹⁹ A complete blood count and B12 levels should be monitored in patients accordingly.

Jalyn™, a new combination product for the treatment of benign prostatic hyperplasia, has been approved for men affected by this condition. It is a combination of dutasteride (Avodart®) and tamsulosin hydrochloride (Flomax®).²⁰

When prescribing Jalyn™, clinicians are reminded to obtain a baseline prostate-specific antigen, or PSA, prior to prescribing the medication and then to reassess the PSA in six months. The PSA

should decrease by 50% of the baseline at the six-month mark due to dutasteride and its mechanism of action. If a 50% reduction is not seen in the PSA level at six months, the clinician should consider referring the patient to urology. The lack of reduction in the PSA after medication initiation may be indicative of an underlying prostate cancer that has gone undetected. Of importance is that the PSA obtained at six months becomes the patient's new baseline PSA and should be used for future comparison.²⁰

Mometasone furoate 100 mcg and formoterol fumarate dehydrate (Dulera[®]), a new combination of an inhaled corticosteroid and long-acting beta2 adrenergic agonist, or LABA, has been approved for the treatment of patients 12 years of age and older with asthma. Delivered via a metered dose inhaler, Dulera[®] is available in two different strengths — 100 mcg/5 mcg and 200 mcg/5 mcg — and should be dosed as two puffs two times daily.²¹ This product joins the market in an increasingly crowded field of such combination products as fluticasone and salmeterol (Advair[®]), and budesonide and formoterol fumarate (Symbicort[®]). Labeling has been updated on all products containing a LABA to reflect the FDA warning regarding short-term use with these products due to the potential to increase the risk of asthma-related deaths. Clinicians are encouraged to utilize LABAs when clinically indicated but to step down the asthma therapy when warranted, based upon the patient's asthma control status.²¹

NEW APPROVALS AND IMPORTANT UPDATES

Fexofenadine HCl (Allegra[®]) has been approved for a prescription-to-over-the-counter switch.²² It currently is sold OTC and joins a competitive field of branded and generic second-generation antihistamine products, such as loratadine (Claritin[®]) and cetirizine (Zyrtec[®]). Duloxetine HCl (Cymbalta[®]) has been approved as a treatment option for patients with chronic musculoskeletal pain.²³ Studies to gain this additional indication were performed on patients with chronic lower back pain and chronic pain due to osteo-

arthritis. For this indication, duloxetine may be initiated at 30 mg and increased to 60 mg once daily as needed. Prior to this additional indication, duloxetine (Cymbalta[®]) already was indicated for major depressive disorder, generalized anxiety disorder, fibromyalgia and diabetic peripheral neuropathic pain.²³

Given the increase in chronic health conditions seen among children, many manufacturers have become more aggressive in seeking indications for children and adolescents. Rosuvastatin calcium (Crestor[®]) is approved to treat heterozygous familial hypercholesterolemia (elevated total cholesterol, low-density lipoprotein and apolipoprotein B) in children and adolescents 10 years to 17 years of age.²⁴ It joins the rank of atorvastatin (Lipitor[®]), which previously had gained FDA approval for the same indications. Colesevelam hydrochloride (Welchol[®]) also is indicated for boys and postmenar-

chal girls ages 10 years to 17 years with heterozygous familial hypercholesterolemia. It should be administered once daily in the powdered version and may be used as monotherapy or co-administered with a HMG-CoA reductase inhibitor (statin).²⁶ Metformin (Glucophage[®]) is approved for children older than 10 years of age with Type 2 diabetes.²⁷ Almotriptan malate (Axert[®]) has received approval for the treatment of migraines in adolescents ages 12 years to 17 years, and olmesartan medoxomil (Benicar[®]) is approved for children ages 6 years to 16 years of age to treat hypertension.^{28,29}

ADDITIONAL UPDATES AND LABELING REVISIONS

Clopidogrel bisulfate (Plavix[®]) now carries a boxed warning regarding reduced efficacy in patients who are poor metabolizers, principally of the CYP2C19 pathway.³⁰ Triamcinolone (Azmecort[®])

Table 1
Medications on the FDA watch list

GENERIC (BRAND)	SAFETY CONCERNS
Benzonatate (Tessalon)	Accidental ingestion causing deaths in children
Dronedarone hydrochloride (Multaq)	Interaction with warfarin (e.g., increased bleeding)
Epoetin alfa (Epogen/Procrit)	Contamination with shards of glass from vial
Gemcitabine hydrochloride (Gemzar)	Liver disease
Lanreotide acetate (Somatuline Depot)	Pancreatitis (hemorrhagic and necrotizing)
Lanthanum carbonate (Fosrenol)	Swallowing problems and gastrointestinal obstruction
Levetiracetam (Keppra)	Stevens-Johnson syndrome
Lithium citrate (Lithobid and Eskalith)	Brugada syndrome
Lopinavir/ritonavir oral solution (Kaletra)	Serious events in neonates
Immune globulin G IV 5% liquid (Octagam)	Thromboembolic events
Pioglitazone HCl (Actos)	Rhabdomyolysis
Ranolazine (Ranexa)	Interaction with statins (e.g., rhabdomyolysis)
Sodium oxybate (Xyrem)	Death

PRACTICE POINTS

- Denosumab (Prolia[™]) is a receptor activator of nuclear factor kappa beta ligand (RANKL) and belongs to a new class of medication indicated for the management of postmenopausal osteoporosis at high risk of fracture.
- Dabigatran etexilate mesylate (Pradaxa[®]) may ultimately replace warfarin (Coumadin[®]) in the future, given the lack of interactions with foods containing vitamin K and no need for international normalized ratio monitoring.
- Guanfacine (Intuniv[®]) is a selective alpha-2A adrenergic receptor agonist and is now approved for the treatment of attention deficit hyperactivity disorder in children and adolescents ages 6 years to 17 years of age.
- Combination therapy has become very common, particularly for patients with hypertension.

is no longer produced in the United States. This discontinuation was not at all related to safety issues with the product itself, but instead was due to the commitment of the United States to phase out all medications containing chlorofluorocarbons, which are believed to be harmful to the ozone.³¹ Nedocromil (Tilade®) and cromolyn (Intal®) metered-dose inhalers also are no longer produced in the United States, and patients on these medications should be transitioned off of them and switched to other medications.³¹ Sibutramine (Meridia®) was voluntarily pulled by its manufacturer in October 2010 after increased consumer and FDA pressure due to studies and reports of increased risk of cardiovascular events.³²

There are new warnings regarding zoledronic acid (Reclast®) and reports to the FDA regarding the development of renal failure following the intravenous

infusion.³³ The majority of these patients responded to intravenous fluids. Patients and clinicians must be made aware of the increased need for hydration before, during and after this infusion.³³ All bisphosphonates now carry a warning regarding increased risk of nontraumatic fractures (subtrochanteric).³⁴ It is important to reassure patients that these fractures constitute approximately 1% of all fractures in patients with osteoporosis. Patients may be reporting to clinicians about hearing that angiotensin receptor blockers, or ARBs, are associated with increased risk of developing lung cancer.³⁵ All of the manufacturers of ARBs already have begun to examine this potential link and continue to look for evidence regarding this in previous and future clinical trials. Propoxyphene (Darvon®, Darvocet®) has been withdrawn from the market due to liver and cardiac tox-

icity.³⁶ In 2010, the FDA added 13 drugs to its watch list for a variety of reasons. Table 1 contains the list of these medications and the reasons for the medications' addition to the FDA watch list.³⁷

WHAT TO EXPECT IN 2011 AND 2012³⁸

Clinicians can expect a busy 2011 and 2012 from an FDA drug approval standpoint. Clinicians can expect Afrezza® (inhaled insulin) for adults with Type 2 diabetes. This product currently is undergoing its second review cycle for approval. Tradjenta® (linagliptin), a new DPP-4 inhibitor for adults with Type 2 diabetes, will join this increasingly expanding class. GlaxoSmithKline will be marketing Horizant® (gabapentin enacarbil) as a treatment for restless leg syndrome. Last, Edarbi® (azilsartan medoxomil), an ARB, will be introduced for the treatment of hypertension in adults.

1 Fiercebitech.com/topics/fda_approval_process.asp. Accessed April 1, 2011. 2 Tektur® (aliskiren) Prescribing Information. Novartis Pharmaceuticals. East Hanover, N.J. Pharma.us.novartis.com/product/pi/pdf/tektur.pdf 3 Prolia™ (denosumab) Prescribing Information. Amgen. 2010. Thousand Oaks, Calif. http://pi.amgen.com/united_states/prolia/pi.pdf. 4 Xgeva™ (denosumab) Prescribing Information. Amgen. 2010. Thousand Oaks, Calif. Xgeva.com 5 Pradaxa® (dabigatran etexilate mesylate) Prescribing Information. Boehringer Ingelheim. 2010. Ridgefield, Conn. Bidocs.boehringer-ingelheim.com/BIWebAccess/ViewServlet.ser?docBase=renetnt&folderPath=/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf 6 Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al. RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. *New England Journal of Medicine*. 2009. 361(12):1139-1151. 7 Victoza® (liraglutide) Prescribing Information. 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New drug update 2011

Learning Assessment

Successful completion of “New drug update 2011” is accredited for 1.4 hours of continuing education credit, of which 1.4 hours are considered pharmacology credit. To obtain credit, answer the following questions and complete the evaluation online at RetailClinician.com.

- To which class of medication does aliskiren (Tekturna®) belong?**
 - ACE inhibitor
 - Beta blocker
 - ARB
 - Direct renin inhibitor
- For which of the following individuals would denosumab (Prolia™) be indicated?**
 - 52-year-old male with diabetes
 - 65-year-old female with osteoporosis
 - 45-year-old female with osteopenia
 - 70-year-old male with hypertension
- Of the following, which is a potential advantage to the use of dabigatran etexilate mesylate (Pradaxa®)?**
 - It is more cost-effective.
 - There is no need for INR monitoring.
 - It has more indications than warfarin (Coumadin®).
 - None of the above
- Liraglutide (Victoza®) should be avoided in patients with a history of what condition?**
 - Thyroid carcinoma
 - Hypertension
 - Glaucoma
 - Coronary artery disease
- Dofetilide (Tikosyn®) should always be initiated in an inpatient setting due to its potential to:**
 - Prolong the PR interval
 - Prolong the QRS interval
 - Increase the heart rate
 - Prolong the QT interval
- In the individual currently taking clarithromycin (Biaxin®), which of the following dosages of vilazodone (VIIBRYD™) should be utilized?**
 - 20 mg once daily
 - 30 mg once daily
 - 40 mg once daily
 - 50 mg once daily
- Prasugrel (Effient®) may be a better option than clopidogrel (Plavix®) for the patient currently taking which concomitant class of medication?**
 - Antacids
 - H2 receptor agonists
 - Proton-pump inhibitors
 - None of the above
- How does guanfacine (Intuniv®) work to improve symptoms in patients with ADHD?**
 - It increases the release of serotonin.
 - It increases the release of dopamine.
 - It increases the release of norepinephrine.
 - The mechanism of action is not known.
- Patients on long-term metformin therapy should be monitored for which of the following?**
 - Leukopenia
 - Vitamin B12 deficiency
 - Thrombocytopenia
 - Elevated liver enzymes
- Which of the following medications is now available to patients without a prescription?**
 - Pravastatin (Pravachol®)
 - Sibutramine (Meridia®)
 - Fexofenadine (Allegra®)
 - Triamcinolone (Azmacort®)