Current FDA-Related Drug Information

Approvals, Submission, and Important Labeling Changes for US Marketed Pharmaceuticals

Danial E. Baker, PharmD, FASHP, FASCP*

This monthly feature will help readers keep current on new drugs, new indications, dosage forms, and safety-related changes in labeling or use. Efforts have been made to ensure the accuracy of this information; however, if there are any questions, please let me know at danial.baker@wsu.edu.

Table 1. New drugs approved by the US Food and Drug Administration (FDA): February 16, 2014 through March 15, 2015

Ceftazidime/avibactam – *Avycaz* (Forest Pharmaceuticals)

<i>Comparative agents:</i>	Ceftazidime; Ceftolozane/tazobactam
<i>Indication:</i>	Treatment of adults with complicated intraabdominal infections, in combination with metronidazole, and complicated urinary tract infections, including pyelonephritis, who have limited or no alternative treatment options
<i>Mechanism of action:</i>	Ceftazidime inhibits bacterial cell wall synthesis. Avibactam is a beta-lactamase inhibitor active against types A, C, and some D beta-lactams.
<i>Common adverse effects:</i>	Vomiting, nausea, constipation, anxiety
<i>Dosage form & strength:</i>	Injection; 2 g ceftazidime/0.5 g avibactam
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206494s000lbl.pdf

Dinutuximab – *Unituxin* (United Therapeutics Corporation)

<i>Comparative agents:</i>	None
<i>Indication:</i>	In combination with granulocyte-macrophage colony-stimulating factor, interleukin-2, and 13-cis-retinoic acid, for the treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy
<i>Mechanism of action:</i>	GD2-binding monoclonal antibody; binds to cell surface GD2 and induces cell lysis of GD2-expressing cells through antibody-dependent cell-mediated cytotoxicity and complement-dependent cytotoxicity
<i>Common adverse effects:</i>	Pain, pyrexia, thrombocytopenia, lymphopenia, infusion reactions, hypotension, hyponatremia, increased alanine aminotransferase, anemia, vomiting, diarrhea, hypokalemia, capillary leak syndrome, neutropenia, urticaria, hypoalbuminemia, increased aspartate aminotransferase, and hypocalcemia
<i>Dosage form & strength:</i>	Injection; 17.5 mg/5 mL single-use vial
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125516s000lbl.pdf

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*Director, Drug Information Center, College of Pharmacy, Washington State University Spokane, PO Box 1495, Spokane, WA 99210-1495.

Table 1. New drugs approved by the US Food and Drug Administration (FDA): February 16, 2014 through March 15, 2015 (CONT.)**Insulin glargine [rDNA origin] – Toujeo (Sanofi)**

<i>Comparative agents:</i>	Insulin glargine U-100
<i>Indication:</i>	Improvement in glycemic control in adults with type 1 and type 2 diabetes
<i>Mechanism of action:</i>	Basal insulin
<i>Common adverse effects:</i>	Hypoglycemia, allergic reactions, injection site reaction, lipodystrophy, pruritus, rash, edema, and weight gain
<i>Dosage form & strength:</i>	Injection; SoloSTAR disposable prefilled pen – U-300 (300 units/mL in 1.5 mL)
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206538lbl.pdf

Isavuconazonium sulfate – Cresemba (Astellas Pharma)

<i>Comparative agents:</i>	Caspofungin, itraconazole, micafungin, posaconazole, voriconazole
<i>Indication:</i>	Treatment of invasive aspergillosis and invasive mucormycosis
<i>Mechanism of action:</i>	Prodrug of isavuconazole, an azole antifungal drug, that inhibits the synthesis of ergosterol and ultimately weakens the membrane structure and function of the fungal cell wall
<i>Common adverse effects:</i>	Nausea, vomiting, diarrhea, headache, elevated liver chemistry tests, hypokalemia, constipation, dyspnea, cough, peripheral edema, and back pain
<i>Dosage form & strength:</i>	Capsules: 186 mg of isavuconazonium sulfate Injection: Single-dose vial with lyophilized powder containing 372 mg of isavuconazonium
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207500Orig1s000lbl.pdf

Levonorgestrel – Liletta (Actavis)

<i>Comparative agents:</i>	Intrauterine systems
<i>Indication:</i>	Prevention of pregnancy for up to 3 years
<i>Mechanism of action:</i>	Prevention of fertilization due to the thickening of the cervical mucus resulting in altered sperm passage and mobility along with alteration of the endometrium
<i>Common adverse effects:</i>	Vaginal and vulvovaginal infections, acne
<i>Dosage form & strength:</i>	Intrauterine system with 52 mg levonorgestrel
<i>Product labeling:</i>	http://pi.actavis.com/data_stream.asp?product_group=1960&p=pi&language=E

Panobinostat – Farydak (Novartis)

<i>Comparative agents:</i>	Belinostat; Vorinostat; Romidepsin
<i>Indication:</i>	In combination with bortezomib and dexamethasone, is indicated for the treatment of patients with multiple myeloma who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent
<i>Mechanism of action:</i>	Histone deacetylase inhibitor
<i>Common adverse effects:</i>	Diarrhea, fatigue, nausea, peripheral edema, decreased appetite, pyrexia, and vomiting
<i>Dosage form & strength:</i>	Capsules; 10, 15, 20 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/205353s000lbl.pdf

Current FDA-Related Drug Information

Table 2. New dosage forms and indications approved by the FDA: February 16, 2015 through March 15, 2015

Generic name	Brand name (Company)	Indication and comments
New indications		
Lenalidomide	<i>Revlimid</i> (Celgene)	Treatment of newly diagnosed patients with multiple myeloma
Nivolumab	<i>Opdivo</i> (Bristol-Myers Squibb)	Treatment of patients with advanced (metastatic) squamous non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy
Rufinamide	<i>Banzel</i> (Eisai)	Treatment of seizures with Lennox-Gastaut Syndrome (LGS) in pediatric patients

Table 3. Agents pending FDA approval: February 16, 2015 through March 15, 2015

Generic name	Brand name (Company)	Indication and comments
Agents scheduled for review by an FDA advisory panel		
Fluticasone furoate/vilanterol inhalation powder	<i>Breo Ellipta</i> (GlaxoSmithKline)	Once daily maintenance treatment of asthma in patients 12 years and older – supplemental new drug application (3/19/15)
Infliximab	CT-P13 (Celltrion)	Biosimilar evaluation & recommendation (3/17/15)
Talimogene laherparepvec	(Amgen)	Treatment of patients with injectable regional or distantly metastatic melanoma

Table 4. New drug/biologics license applications filed by manufacturer: February 16, 2015 through March 15, 2015

Generic name Brand name (Company)	Comparative agents	Indication	Mechanism of action	Common adverse effects	Dosage form or route	Comments
Ciprofloxacin <i>AuriPro</i> (Otonomy)	Ciprofloxacin, oral	Treatment of middle ear effusions in pediatric patients undergoing tympanostomy tube placement surgery	Antibiotic	N/A	Otic drops; sustained-release	Single dose administration

Table 5. Significant labeling changes or “Dear Health Professional” letters related to safety^a

Generic name Brand name (Company)	Warning
Degarelix <i>Firmagon</i> (Ferring)	<p>WARNINGS AND PRECAUTIONS</p> <p>Effect on QT/QTc Interval</p> <ul style="list-style-type: none"> Androgen deprivation therapy may prolong the QT interval. Providers should consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, frequent electrolyte abnormalities, and in patients taking drugs known to prolong the QT interval. Electrolyte abnormalities should be corrected. Consider periodic monitoring of electrocardiograms and electrolytes. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm346725.htm</p>
Desflurane <i>Suprane</i> (Baxter Healthcare Corporation)	<p>CONTRAINDICATIONS</p> <ul style="list-style-type: none"> Patients with a history of moderate to severe hepatic dysfunction following anesthesia with desflurane or other halogenated agents and not otherwise explained. <p>WARNINGS AND PRECAUTIONS</p> <p>Malignant Hyperthermia</p> <ul style="list-style-type: none"> Fatal outcome of malignant hyperthermia has been reported with desflurane. <p>Respiratory Adverse Reactions in Pediatric Patients</p> <ul style="list-style-type: none"> Children, particularly if 6 years old or younger, are at increased risk for adverse respiratory reactions, eg, coughing and laryngospasm, especially with removal of the laryngeal mask airway under deep anesthesia. Closely monitor these patients for signs and symptoms associated with laryngospasm and treat accordingly. In children with asthma or a history of recent upper airway infection, there is an increased risk for airway narrowing and increases in airway resistance. Closely monitor these patients for signs and symptoms associated with airway narrowing and treat accordingly. <p>ADVERSE REACTIONS</p> <p>Cardiac Disorders: Atrial fibrillation</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm372692.htm</p>
Exenatide <i>Byetta</i> (AstraZeneca)	<p>Labeling changed to emphasize that these devices must never be shared between patients, even if the needle is changed. Sharing poses a risk for transmission of blood-borne pathogens.</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm437267.htm</p>
Galantamine hydrobromide tablets, oral solution, and ER capsules <i>Razadyne & Razadyne ER</i> (Janssen)	<p>Serious skin reactions (Stevens–Johnson syndrome and acute generalized exanthematous pustulosis) have been reported. If signs or symptoms suggest a serious skin reaction, use of this drug should not be resumed and alternative therapy should be considered.</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm299522.htm</p>
Goserelin acetate <i>Zoladex</i> (AstraZeneca)	<p>WARNINGS AND PRECAUTIONS</p> <p>Injection Site Injury</p> <ul style="list-style-type: none"> Injection site injury and vascular injury including pain, hematoma, hemorrhage, and hemorrhagic shock, requiring blood transfusions and surgical intervention, have been reported with <i>Zoladex</i>. Extra care should be taken when administering <i>Zoladex</i> to patients with low body mass index and/or to patients receiving full dose anticoagulation. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm182245.htm</p>
Insulin pens (Various)	<p>Labeling changed to emphasize that these devices must never be shared between patients, even if the needle is changed. Sharing poses a risk for transmission of blood-borne pathogens.</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm437267.htm</p>
Lamivudine <i>EpiVir</i> (GlaxoSmithKline)	<p>Avoid using with other products that contain any of the active ingredients.</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm437293.htm</p>

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Table 5. Significant labeling changes or “Dear Health Professional” letters related to safety^a (CONT.)

Generic name Brand name (Company)	Warning
Liraglutide [rDNA origin] injection <i>Victoza</i> (Novo Nordisk)	Labeling changed to emphasize that these devices must never be shared between patients, even if the needle is changed. Sharing poses a risk for transmission of blood-borne pathogens. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm437267.htm
Minocycline <i>Minocin</i> (Precision Dermat)	WARNINGS Intracranial Hypertension <ul style="list-style-type: none"> Intracranial hypertension (IH, pseudotumor cerebri) has been associated with the use of tetracyclines including <i>Minocin</i>. Clinical manifestations of IH include headache, blurred vision, diplopia, and vision loss; papilledema can be found on funduscopy. Women of childbearing age who are overweight or have a history of IH are at greater risk. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm437541.htm
Ospemifene <i>Osphena</i> (Shionogi)	CONTRAINDICATION: Hypersensitivity to the drug or any product ingredients ADVERSE REACTIONS - POSTMARKETING EXPERIENCE: Allergic conditions including hypersensitivity, angioedema, rashes, pruritis, urticarial http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm437542.htm
Oxybutynin chloride <i>Ditropan XL</i> (Janssen)	WARNINGS AND PRECAUTIONS Central Nervous System Effects <ul style="list-style-type: none"> <i>Ditropan XL</i> should be used with caution in patients with Parkinson’s disease due to the risk of aggravation of symptoms. Worsening of Symptoms of Decreased Gastrointestinal Motility in Patients with Autonomic Neuropathy <ul style="list-style-type: none"> <i>Ditropan XL</i> should be used with caution in patients with autonomic neuropathy due to the risk of aggravation of symptoms of decreased gastrointestinal motility. DRUG INTERACTIONS <ul style="list-style-type: none"> Anticholinergic agents may also antagonize the effects of prokinetic agents, such as metoclopramide. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm262576.htm
Pramlintide acetate <i>Symlin</i> (AstraZeneca)	Labeling changed to emphasize that these devices must never be shared between patients, even if the needle is changed. Sharing poses a risk for transmission of blood-borne pathogens. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm437267.htm
Prazosin <i>Minipress</i> (Pfizer)	WARNINGS: Priapism <ul style="list-style-type: none"> Prolonged erections and priapism have been reported with alpha-1 blockers. In the event of an erection that persists longer than 4 hours, seek immediate medical assistance. If priapism is not treated immediately, penile tissue damage and permanent loss of potency could result. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm437379.htm
Rivastigmine tartrate <i>Exelon</i> capsule & solution (Novartis)	WARNINGS AND PRECAUTIONS Allergic Dermatitis <ul style="list-style-type: none"> Isolated reports of patients experiencing disseminated allergic dermatitis when administered rivastigmine irrespective of the route of administration (oral or transdermal). Treatment should be discontinued if disseminated allergic dermatitis occurs. ADVERSE REACTIONS <ul style="list-style-type: none"> Skin and Appendages: Disseminated allergic dermatitis. DRUG INTERACTIONS Metoclopramide <ul style="list-style-type: none"> Due to the risk of additive extrapyramidal adverse reactions, the concomitant use of metoclopramide and rivastigmine is not recommended.

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Table 5. Significant labeling changes or “Dear Health Professional” letters related to safety^a (CONT.)

Generic name Brand name (Company)	Warning
	<p>Cholinomimetic and Anticholinergic Medications</p> <ul style="list-style-type: none"> Rivastigmine may increase the cholinergic effects of other cholinomimetic medications and may also interfere with the activity of anticholinergic medications (eg, oxybutynin, tolterodine). Concomitant use of rivastigmine with medications having these pharmacologic effects is not recommended unless deemed clinically necessary. <p>Beta-blockers</p> <ul style="list-style-type: none"> Additive bradycardic effects resulting in syncope may occur when rivastigmine is used concomitantly with beta-blockers, especially cardioselective beta-blockers (including atenolol). Concomitant use of rivastigmine with beta-blockers is not recommended. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm373593.htm</p>
Rivastigmine tartrate <i>Exelon</i> patch (Novartis)	<p>WARNINGS AND PRECAUTIONS</p> <p>Skin Reactions</p> <ul style="list-style-type: none"> Skin application site reactions may occur with <i>Exelon</i> patch. These reactions are not in themselves an indication of sensitization. However, use of rivastigmine patch may lead to allergic contact dermatitis. There have been isolated postmarketing reports of patients experiencing disseminated allergic dermatitis when administered rivastigmine irrespective of the route of administration (oral or transdermal). <p>ADVERSE REACTIONS</p> <ul style="list-style-type: none"> Disseminated allergic dermatitis, tremor. <p>DRUG INTERACTIONS</p> <p>Metoclopramide</p> <ul style="list-style-type: none"> Due to the risk of additive extrapyramidal adverse reactions, the concomitant use of metoclopramide and rivastigmine is not recommended. <p>Cholinomimetic and Anticholinergic Medications</p> <ul style="list-style-type: none"> Rivastigmine may increase the cholinergic effects of other cholinomimetic medications and may also interfere with the activity of anticholinergic medications (eg, oxybutynin, tolterodine). Concomitant use of rivastigmine with medications having these pharmacologic effects is not recommended unless deemed clinically necessary. <p>Beta-blockers</p> <ul style="list-style-type: none"> Additive bradycardic effects resulting in syncope may occur when rivastigmine is used concomitantly with beta-blockers, especially cardioselective beta-blockers (including atenolol). Concomitant use of rivastigmine with beta-blockers is not recommended. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm360439.htm</p>
Rotigotine <i>Neupro</i> patch transdermal system (UCB)	<p>WARNINGS AND PRECAUTIONS</p> <p>Symptomatic Hypotension</p> <ul style="list-style-type: none"> An increased risk for decreases in systolic and diastolic blood pressure were observed when supine, standing, and changing from supine to standing position in patients treated with rotigotine. <p>Syncope</p> <ul style="list-style-type: none"> Patients with severe cardiovascular disease should be asked about symptoms of syncope and pre-syncope. <p>Elevation of Blood Pressure and Heart Rate</p> <ul style="list-style-type: none"> Some patients treated with rotigotine exhibited increases in systolic blood pressure (>180 mm Hg) and/or diastolic blood pressure (>105 mm Hg) while supine or standing.

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Table 5. Significant labeling changes or “Dear Health Professional” letters related to safety^a (CONT.)

Generic name <i>Brand name</i> (Company)	Warning
	<p>Weight Gain and Fluid Retention</p> <ul style="list-style-type: none"> In patients taking the maximum recommended rotigotine dose, the incidence of peripheral edema may be increased. Monitor for weight gain and fluid retention when treating patients with concomitant illnesses such as congestive heart failure or renal insufficiency. <p>Dyskinesia</p> <ul style="list-style-type: none"> Rotigotine exhibited a dose-dependent relationship for all doses and the risk of developing dyskinesia. <p>ADVERSE REACTIONS</p> <p>Laboratory Changes</p> <ul style="list-style-type: none"> Increased risk for low hemoglobin, decreased hematocrit, elevated serum blood urea nitrogen (BUN), low serum glucose, and increased serum creatine phosphokinase (CPK) compared to placebo therapy. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm302528.htm</p>
Testosterone products (Various)	<p>Labeling needs to better clarify the products approved use(s) and the risk of heart attacks and strokes in patients taking testosterone. Prescribers should limit their use of these products to men with low testosterone levels caused by certain medical conditions and confirmed by laboratory tests.</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm436280.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery</p>
Varenicline <i>Chantix</i> (Pfizer)	<p>Caution with alcohol, the combination may increase drunkenness, unusual or aggressive behavior, no memory of things that happened, or seizures.</p> <p>http://www.fda.gov/Drugs/DrugSafety/ucm436494.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery</p>
Voriconazole <i>VFEND</i> (Pfizer)	<p>WARNINGS AND PRECAUTIONS</p> <p>Hepatic Toxicity</p> <ul style="list-style-type: none"> Measure serum transaminase levels and bilirubin at the initiation of voriconazole therapy and monitor at least weekly for the first month of treatment. Monitoring frequency can be reduced to monthly during continued use if no clinically significant changes are noted. If liver function tests become markedly elevated compared to baseline, voriconazole should be discontinued unless the medical judgment of the benefit-risk of the treatment for the patient justifies continued use. <p>Arrhythmias and QT Prolongation</p> <ul style="list-style-type: none"> Voriconazole should be administered with caution to patients with potentially proarrhythmic conditions, such as patients with congenital or acquired QT-prolongation; cardiomyopathy, in particular when heart failure is present; sinus bradycardia; those with existing symptomatic arrhythmias; or concomitant medicinal product that is known to prolong QT interval. Rigorous attempts to correct potassium, magnesium, and calcium should be made before starting and during voriconazole therapy. <p>Dermatological Reactions</p> <ul style="list-style-type: none"> Voriconazole has been associated with photosensitivity skin reaction. Measures such as protective clothing and sunscreen with high sun protection factor (SPF) should be recommended. The frequency of phototoxicity reactions is higher in the pediatric population. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm283035.htm</p>

^aPractitioners are encouraged to check the US Food and Drug Administration's MEDWATCH Web site (<http://www.fda.gov/medwatch/safety.htm>) for updated information.