Current FDA-Related Drug Information

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

Daniel 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 daniel.baker@wsu.edu.

Table 1. New drugs approved by the US Food and Drug Administration (FDA): May 15, 2014 through July 14, 2014

Antihemophilic Factor (Recombinant), Fc Fusion Protein – ELOCTATE (Biogen Idec)	
<i>Comparative agents:</i>	Antihemophilic factor for hemophilia A (congenital Factor VIII deficiency)
<i>Indication:</i>	Hemophilia A (congenital Factor VIII deficiency), adults and children, for control and prevention of bleeding episodes; perioperative management; and routine prophylaxis to prevent or reduce the frequency of bleeding episodes.
<i>Mechanism of action:</i>	Replacement antihemophilic factor
<i>Common adverse effects:</i>	Arthralgia and malaise
<i>Dosage form & strength:</i>	Injection; 250, 500, 750, 1000, 1500, 2000, or 3000 international units of Factor VIII potency/vial
<i>Product labeling:</i>	http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/UCM400192.pdf
Belinostat – Beleodaq (Spectrum Pharmaceuticals)	
<i>Comparative agents:</i>	Vorinostat
<i>Indication:</i>	Treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)
<i>Mechanism of action:</i>	Histone deacetylase inhibitor
<i>Common adverse effects:</i>	Nausea, fatigue, pyrexia, anemia, and vomiting
<i>Dosage form & strength:</i>	Injection; 500 mg
<i>Product labeling:</i>	http://www.sppirx.com/downloads/140703_final-beleodaq-pi-pt-info.pdf

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

Buprenorphine/Naloxone – *Bunavail* (BioDelivery Sciences International)

<i>Comparative agents:</i>	Buprenorphine
<i>Indication:</i>	Maintenance treatment of opioid dependence
<i>Mechanism of action:</i>	Partial opioid agonist/opioid antagonist
<i>Common adverse effects:</i>	Headache, nausea, vomiting, hyperhidrosis, constipation, signs and symptoms of withdrawal, insomnia, pain
<i>Dosage form & strength:</i>	Buccal film; 2.1 mg/0.3 mg; 4.2 mg/0.7 mg/6.3 mg/1 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205637s000lbl.pdf

Dalbavancin – *Dalvance* (Durata Therapeutics)

<i>Comparative agents:</i>	Vancomycin
<i>Indication:</i>	Acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible strains of Gram-positive microorganisms
<i>Mechanism of action:</i>	Interferes with cell wall synthesis by binding to the D-alanyl-D-alanine terminus of the stem pentapeptide in nascent cell wall peptidoglycan which then prevents it from cross-linking
<i>Common adverse effects:</i>	Nausea, diarrhea, headache
<i>Dosage form & strength:</i>	Injection: 500 mg single-use vial
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/021883s000lbl.pdf

Efinaconazole – *Jublia* (Dow Pharm)

<i>Comparative agents:</i>	Clotrimazole, econazole, ketoconazole
<i>Indication:</i>	Topical treatment of onychomycosis of the toenails due to <i>Trichophyton rubrum</i> and <i>Trichophyton mentagrophytes</i>
<i>Mechanism of action:</i>	Inhibits fungal lanosterol 14 α -demethylase involved in the biosynthesis of ergosterol and altering the fungal cell membranes
<i>Common adverse effects:</i>	Ingrown toenails, application site dermatitis, application site vesicles, and application site pain
<i>Dosage form & strength:</i>	Solution; 10%
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/203567s000lbl.pdf

Insulin – *Afrezza* (MannKind Corporation)

<i>Comparative agents:</i>	Insulin, injectable
<i>Indication:</i>	Improve glycemic control in adult patients with diabetes mellitus
<i>Mechanism of action:</i>	Hormone replacement
<i>Common adverse effects:</i>	Hypoglycemia, cough, throat pain, and irritation
<i>Dosage form & strength:</i>	Inhalation powder; 4 units & 8 units
<i>Product labeling:</i>	http://www.mannkindcorp.com/Collateral/Documents/English-US/Afrezza_PrescribingInformation.pdf

Phenylephrine/Ketorolac – Omidria (Omeros)

<i>Comparative agents:</i>	Individual ingredients
<i>Indication:</i>	Maintaining pupil size by preventing intraoperative miosis and reducing postoperative pain during cataract surgery or intraocular lens replacement
<i>Mechanism of action:</i>	Alpha 1-adrenergic receptor agonist and nonselective cyclooxygenase inhibitor
<i>Common adverse effects:</i>	Eye irritation, posterior capsule opacification, increased intraocular pressure, and anterior chamber inflammation
<i>Dosage form & strength:</i>	Ocular solution concentrate; 1% w/v phenylephrine and 0.3% w/v ketorolac
<i>Product labeling:</i>	http://www.omidria.com/OMIDRIA-Prescribing-Information.pdf

Tavaborole – Kerydin (Anacor Pharmaceuticals)

<i>Comparative agents:</i>	Topical antifungals
<i>Indication:</i>	Topical treatment of onychomycosis of the toenails due to <i>Trichophyton rubrum</i> or <i>Trichophyton mentagrophytes</i>
<i>Mechanism of action:</i>	Inhibition of fungal protein synthesis by inhibition of aminoacyl-transfer ribonucleic acid (tRNA) synthetase (AARS)
<i>Common adverse effects:</i>	Application site exfoliation, ingrown toenail, application site erythema, and application site dermatitis
<i>Dosage form & strength:</i>	Solution; 5%
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/204427s000lbl.pdf

Tedizolid phosphate – Sivextro (Cubist Pharmaceuticals)

<i>Comparative agents:</i>	Linezolid
<i>Indication:</i>	Adults for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria
<i>Mechanism of action:</i>	Binding to the 50S subunit of the bacterial ribosome resulting in inhibition of protein synthesis
<i>Common adverse effects:</i>	Nausea, headache, diarrhea, vomiting, and dizziness
<i>Dosage form & strength:</i>	Injection and tablets; 200 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205435s000lbl.pdf

Testosterone – Natesto Nasal Gel (Trimel Pharmaceuticals)

<i>Comparative agents:</i>	Testosterone
<i>Indication:</i>	Replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone: primary hypogonadism (congenital or acquired) and hypogonadotropic hypogonadism (congenital or acquired)
<i>Mechanism of action:</i>	Androgen replacement
<i>Common adverse effects:</i>	Prostate specific antigen increased, headache, rhinorrhea, epistaxis, nasal discomfort, nasopharyngitis, bronchitis, upper respiratory tract infection, sinusitis, and nasal scab
<i>Dosage form & strength:</i>	Nasal; metered-dose pump (5.5 mg/actuation)
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205488s000lbl.pdf

Vedolizumab – Entyvio (Takeda Pharmaceuticals American, Inc.)	
<i>Comparative agents:</i>	Natalizumab
<i>Indication:</i>	Treatment for adults with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids for inducing and maintaining clinical response; inducing and maintaining clinical remission; improving endoscopic appearance of the mucosa; or achieving corticosteroid-free remission. Vedolizumab is also approved for the treatment of adults with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids for achieving clinical response, achieving clinical remission, or achieving corticosteroid-free remission.
<i>Mechanism of action:</i>	Antagonizes the alpha-4 beta-7 integrin and inhibits binding of the alpha-4 beta-7 integrin to the intestinal mucosal addressin cell adhesion molecule 1 (MAdCAM-1)
<i>Common adverse effects:</i>	Headache, nausea, arthralgia, pyrexia, upper respiratory tract infection, nasopharyngitis, bronchitis, influenza, sinusitis, cough, oropharyngeal pain, fatigue, back pain, rash, pruritus, pain in extremities, and exacerbation of the treated condition
<i>Dosage form & strength:</i>	Injection; 300 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125476s000lbl.pdf

Table 2. New dosage forms and indications approved by the FDA: May 15, 2014 through July 14, 2014

Generic name	Brand name (Company)	Indication and comments
New dosage forms/strength/ route of administration		
Vitamin B-12	<i>Nascobal</i> spray (Strativa)	New single-use device that does not requiring priming
New indications		
Panitumumab	<i>Vectibix</i> (Amgen)	Use in combination with FOLFOX as first-line treatment in patients with wild-type KRAS (exon 2) metastatic colorectal cancer (mCRC).
Coagulation factor VIIa [recombinant]	<i>NovoSeven RT</i> (Novo Nordisk)	Treatment of bleeding episodes and perioperative management in patients with Glanzmann's thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets

Table 3. Agents pending FDA approval: May 15, 2014 through July 14, 2014

Generic name	Brand name (Company)	Indication and comments
Complete response letter: more information required		
Serelaxin	(Novartis)	Additional efficacy information in patients with acute heart failure
Delayed decision by the FDA		
Ferric citrate	(Keryx Biopharmaceuticals)	PDUFA goal date moved to September 7, 2014 to allow the review of supplemental information regarding the drug's chemistry, manufacturing, and controls.
FDA advisory panel: more information required		
Olaparib	(AstraZeneca)	Committee voted 11 to 2 that the current evidence does not support an accelerated approval for use as maintenance treatment for women with platinum-sensitive relapsed ovarian cancer who have the germline BRCA mutation and who are in complete or partial response to platinum-based chemotherapy.
Agents scheduled for review by an FDA advisory panel		
Varenicline tartrate	<i>Chantix</i> (Pfizer)	Review of the risk of serious neuropsychiatric adverse events during a joint meeting of Psychopharmacologic Drugs and the Drug Safety and Risk Management Advisory Committees

Table 4. New drug/biologics license applications filed by manufacturer: May 15, 2014 through July 14, 2014

Generic name Brand name (Company)	Comparative agents	Indication	Mechanism of action	Common adverse effects	Dosage form or route	Comments
Panobinostat (Novartis)	None	Multiple myeloma	Histone and non-histone deacetylase inhibitor; non-selective, resulting in cellular stress and death of the cancer cell	Fatigue, nausea, vomiting, diarrhea, myelosuppression	Intravenous	Granted priority review status by the FDA; adjunctive therapy with other agents for patients with relapsed or relapsed and refractory multiple myeloma

(continued)

Table 4. New drug/biologics license applications filed by manufacturer: May 15, 2014 through July 14, 2014 (CONT.)

Generic name <i>Brand name</i> (Company)	Comparative agents	Indication	Mechanism of action	Common adverse effects	Dosage form or route	Comments
Safinamide (Newron Pharmaceuticals)	None	Adjunctive therapy for patients with early Parkinson's disease treated with stable dose of single dopamine agonist OR those treated with levodopa alone or in combination with other Parkinson's disease treatments in patients with mid- to late stage Parkinson's disease	Reversible inhibition of MAO-B and of dopamine uptake AND inhibition of excessive release of glutamate	Nausea, headache, upper abdominal pain, vomiting, pyrexia, cough, hypertension, blurred vision, gastritis, peripheral edema, nasopharyngitis, dizziness, back pain, tremor	Tablet	

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

Generic name <i>Brand name</i> (Company)	Warning
Acitretin <i>Soriatane</i> (Stiefel)	Angioedema, urticarial hypersensitivity added to Contraindication section. Capillary leak syndrome, exfoliative dermatitis/erythroderma added to Warning section. Immune system disorders, madarosis and exfoliative dermatitis, and vascular disorders added to Adverse Reaction section.
Avanafil <i>Stendra</i> (VIVUS)	Sudden loss of vision in one or both eyes added to the Warnings and Precaution section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm397293.htm
Belimumab <i>Benlysta</i> (GlaxoSmithKline)	Risk of Progressive Multifocal Leukoencephalopathy (PML) in patients with Systemic Lupus Erythematosus (SLE) added to Warnings and Precautions, Patient Counseling Information, and Medication Guide sections. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm299628.htm
Darunavir <i>Prezista</i> (Janssen Products)	Severe skin reaction added to Warning and Precaution section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm287579.htm

(continued)

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

Generic name <i>Brand name</i> (Company)	Warning
Exenatide extended-release <i>Bydureon</i> (AstraZeneca)	Warnings and Precautions: Injection-Site Reactions Postmarketing reports of serious injection-site reactions (eg, abscess, cellulitis, and necrosis), with or without subcutaneous nodules, with the use of <i>Bydureon</i> . Isolated cases required surgical intervention. Adverse Reactions: Postmarketing Experience Allergy/Hypersensitivity: Injection-site reactions Patient Counseling Information: Risk of Injection-Site Reactions Inform patients that there have been postmarketing reports of serious injection-site reactions with or without subcutaneous nodules, with the use of <i>Bydureon</i> . Isolated cases of injection-site reactions required surgical intervention. Advise patients to seek medical advice if symptomatic nodules occur, or for any signs or symptoms of abscess, cellulitis, or necrosis. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm400570.htm
Extended release – long-acting opioid analgesics (Various)	Major rewrite of the Box Warning; Indications and Usage; Warnings and Precautions; Drug Interactions; Use in Specific Populations; and Patient Counseling Information sections related to addiction, abuse, misuse, life-threatening respiratory depression, neonatal opioid withdrawal syndrome, and interactions with alcohol, other CNS depressants, and cytochrome P450 isoenzymes. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm396503.htm
Fingolimod <i>Gilenya</i> (Novartis)	Posterior reversible encephalopathy syndrome added to the Warnings and Precautions section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm266123.htm
Linagliptin <i>Tradjenta</i>	Contraindications Contraindicated in patients with a history of a hypersensitivity reaction to linagliptin, such as anaphylaxis, angioedema, exfoliative skin conditions, urticaria, or bronchial hyperreactivity.
Linagliptin/Metformin hydrochloride <i>Jentadueto</i> (Boehringer Ingelheim Pharmaceuticals)	Warnings and Precautions: Hypersensitivity Reactions There have been postmarketing reports of serious hypersensitivity reactions in patients treated with linagliptin. These reactions include anaphylaxis, angioedema, and exfoliative skin conditions. Onset of these reactions occurred within the first 3 months after initiation of treatment with linagliptin, with some reports occurring after the first dose. Adverse Reactions: Postmarketing Experience Hypersensitivity reactions including anaphylaxis, angioedema, and exfoliative skin conditions Patient Counseling Information Inform patients that serious allergic reactions, such as anaphylaxis, angioedema, and exfoliative skin conditions, have been reported during postmarketing use of linagliptin. If symptoms of allergic reactions (such as rash, skin flaking or peeling, urticaria, swelling of the skin, or swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing) occur, patients must stop taking <i>Tradjenta</i> or <i>Jentadueto</i> and seek medical advice promptly. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm360497.htm
Pegaspargase <i>Oncaspar</i> (Sigma-Tau Pharmaceuticals)	Hepatotoxicity and abnormal liver function added to Warnings and Precautions section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm396543.htm
Rilpivirine <i>Edurant</i> (Janssen)	Rifampin and rifapentine added to the Contraindications and Drug Interactions sections. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm318459.htm
Rosiglitazone maleate products <i>Avandia</i> , <i>Avandamet</i> , <i>Avandaryl</i> (GlaxoSmithKline)	Contraindicated in patients with a history of a hypersensitivity reaction to rosiglitazone or any of the product's ingredients http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm258801.htm

(continued)

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

Generic name <i>Brand name</i> (Company)	Warning
Sapropterin dihydrochloride <i>Kuvan</i> (BioMarin)	Hypophenylalaninemia information update in the Warnings and Precautions section http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm396538.htm
Tadalafil <i>Adcirca & Cialis</i> (Eli Lilly and Company)	Sudden loss of vision in one or both eyes added to the Warnings and Precaution section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm396467.htm http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm203554.htm
Temozolomide <i>Temodar</i> (Merck)	Warnings and Precautions: Hepatotoxicity...section added Fatal and severe hepatotoxicity has been reported. Perform liver function tests at baseline, midway through the first cycle, prior to each subsequent cycle, and approximately 2 to 4 weeks after the last dose of temozolomide. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm211909.htm
Tipranavir <i>Aptivus</i> (Boehringer Ingelheim Pharmaceuticals)	Pimozide drug interaction added to Contraindication section and information related drug interactions with etravirine, rilpivirine, boceprevir, telaprevir, quetiapine, and colchicine added to the Drug Interaction section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/Safety-RelatedDrugLabelingChanges/ucm119931.htm
Vardenafil hydrochloride <i>Levitra</i> (Bayer HealthCare Pharmaceuticals)	Sudden loss of vision in one or both eyes added to the Warnings and Precaution section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/Safety-RelatedDrugLabelingChanges/ucm116474.htm
Vardenafil hydrochloride <i>Staxyn</i> (Bayer HealthCare Pharmaceuticals)	Sudden loss of vision in one or both eyes added to the Warnings and Precaution section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm396800.htm
Vilazodone hydrochloride <i>Viibryd</i> (Forest Laboratories)	Serotonin syndrome added to Warnings and Precaution section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm335517.htm
Voriconazole <i>Vfend</i> (Pfizer)	Drug interaction with efavirenz 400 mg q24h or higher was added to Contraindication section. Everolimus added to the Drug Interaction section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm283035.htm
Zoledronic acid <i>Zometa</i> (Novartis)	Hypocalcemia added to Warnings and Precautions section. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm396804.htm

^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. ■