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): April 16, 2014 through May 15, 2014

Ceritinib – Zykadia (Novartis)	
<i>Comparative agents:</i>	Crizotinib
<i>Indication:</i>	Treatment of patients with anaplastic lymphoma kinase-positive (ALK+) metastatic non-small-cell lung cancer (NSCLC) who were previously treated with crizotinib
<i>Mechanism of action:</i>	ALK tyrosine kinase inhibitor that blocks proteins that promotes the development of cancerous cells
<i>Common adverse effects:</i>	Diarrhea, nausea, vomiting, and abdominal pain
<i>Dosage form & strength:</i>	Capsules; 150 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205755s000lbl.pdf
Omega-3-carboxylic acids – Epanova (AstraZeneca)	
<i>Comparative agents:</i>	Fish-oil products
<i>Indication:</i>	Adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (>500 mg/dL) hypertriglyceridemia
<i>Mechanism of action:</i>	Unknown
<i>Common adverse effects:</i>	Diarrhea, nausea, abdominal pain or discomfort, and eructation
<i>Dosage form & strength:</i>	Capsule; 1 g
<i>Product labeling:</i>	http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#labelinfo

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

Ragweed – Ragwitek (Merck)

<i>Comparative agents:</i>	Compounded desensitizing injections
<i>Indication:</i>	Treat short ragweed (<i>Ambrosia artemisiifolia</i>) pollen-induced allergic rhinitis (hay fever), with or without conjunctivitis (eye inflammation), in adults 18 years through 65 years of age
<i>Mechanism of action:</i>	Desensitization
<i>Common adverse effects:</i>	Throat irritation, oral pruritus, ear pruritus, oral paraesthesia, mouth edema, and tongue pruritus
<i>Dosage form & strength:</i>	Tablet; 12 Amb a 1-Unit
<i>Product labeling:</i>	http://www.fda.gov/downloads/BiologicsBloodVaccines/Allergenics/UCM393600.pdf

Ramucirumab – Cyramza (Eli Lilly)

<i>Comparative agents:</i>	Bevacizumab
<i>Indication:</i>	Treatment of patients with advanced or metastatic, gastric or gastroesophageal junction (GEJ) adenocarcinoma with disease progression on or after prior treatment with fluoropyrimidine- or platinum-containing chemotherapy
<i>Mechanism of action:</i>	Recombinant monoclonal antibody of the IgG1 class that binds to vascular endothelial growth factor receptor-2 (VEGFR-2) and blocks the activation of the receptor that results in a reduction in new blood vessels to the tumor
<i>Common adverse effects:</i>	Hypertension and diarrhea
<i>Dosage form & strength:</i>	Injection; 100 mg/10 mL and 500 mg/50 mL single-dose vials
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/1254771bl.pdf

Siltuximab – Sylvant injection (Janssen Biotech)

<i>Comparative agents:</i>	None
<i>Indication:</i>	Treatment of patients with multicentric Castleman's disease (MCD) who are human immunodeficiency virus-negative (HIV-) and human herpes virus-8-negative (HHV-8)
<i>Mechanism of action:</i>	Binds human IL-6 and prevents the binding of IL-6 to both soluble and membrane-bound IL-6 receptors
<i>Common adverse effects:</i>	Pruritus, increased weight, rash, hyperuricemia, and upper respiratory tract infection
<i>Dosage form & strength:</i>	Injection; 100 mg and 400 mg single-use vials (lyophilized powder)
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125496s000lbl.pdf

Umeclidinium – Incruse Ellipta (GlaxoSmithKline)

<i>Comparative agents:</i>	Anoro Ellipta, Breo Ellipta
<i>Indication:</i>	Long-term treatment of chronic obstructive pulmonary disease (COPD)
<i>Mechanism of action:</i>	Long-acting muscarinic antagonist
<i>Common adverse effects:</i>	Nasopharyngitis, upper respiratory tract infection, cough, arthralgia
<i>Dosage form & strength:</i>	Inhalation powder; 62.5 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205382s000lbl.pdf

Vorapaxar – Zontivity (Merck)	
<i>Comparative agents:</i>	Warfarin
<i>Indication:</i>	Reduction of thrombotic cardiovascular events in patients with a history of myocardial infarction (MI) or with peripheral arterial disease (PAD). Vorapaxar has been shown to reduce the rate of a combined endpoint of cardiovascular death, MI, stroke, and urgent coronary revascularization (UCR).
<i>Mechanism of action:</i>	Protease-activated receptor-1 (PAR-1) antagonist
<i>Common adverse effects:</i>	Bleeding
<i>Dosage form & strength:</i>	Tablet; 2.08 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/204886s000lbl.pdf

---

Table 2. New dosage forms and indications approved by the FDA: April 16, 2014 through May 15, 2014

Generic name	Brand name (Company)	Indication and comments
New dosage forms/ strength/route of administration		
Mercaptopurine	<i>Purixan</i> (NOVA Laboratories Ltd)	20 mg/mL oral suspension for use in the treatment of patients with acute lymphoblastic leukemia
New indications		
Antihemophilic factor VIII	<i>Kogenate FS</i> (Bayer)	Prophylaxis to prevent or reduce the frequency of bleeding episodes in adults with hemophilia A
Ofatumumab	<i>Arzerra</i> injection (GlaxoSmithKline)	Treatment, in combination with chlorambucil, of previously untreated patients with chronic lymphocytic leukemia (CLL), for whom fludarabine-based therapy is considered inappropriate.

Table 3. Agents pending FDA approval: April 16, 2014 through May 15, 2014

Generic name	Brand name (Company)	Indication and comments
Complete response letter: More information required		
Diazepam	<i>Plumiaz</i> (Acorda Therapeutics)	Treatment of patients with epilepsy who experience cluster seizures; NDA “cannot be approved in its present form.”
Recommended for NON- approval by an FDA advisory panel		
Montelukast sodium	<i>Singulair</i> (Merck)	No to Prescription-to-Over-the-Counter classification
Oxycodone/morphine	<i>Moxduo</i> (QRxPharma)	Unanimous vote against approval because the combination agent offered no advantage over the use of oxycodone and morphine.
Agents scheduled for review by an FDA advisory panel		
Olaparib	(AstraZeneca)	Treatment of adult patients with germline BRCA mutation who are in response (complete response or partial response) to platinum-based chemotherapy
Varenicline	<i>Chantix</i> (Pfizer)	Review of the risk of serious neuropsychiatric adverse events associated with varenicline therapy

---

Table 4. New drug/biologics license applications filed by manufacturer: April 16, 2014 – May 15, 2014

Generic name Brand name (Company)	Comparative agents	Indication	Mechanism of action	Common adverse effects	Dosage form or route	Comments
ABT-450 / ritonavir / ombitasvir plus dasabuvir with or without ribavirin (weight-based) (AbbVie/Enanta Pharma)	Sofosbuvir / ribavirin	Treatment of patients with chronic genotype 1 hepatitis C virus (HCV) infection	ABT-450: HCV NS3/4A protease inhibitor; ritonavir: inhibitor of the cytochrome P-450 CYP3A4; ombitasvir: HCV NS5A inhibitor; dasabuvir: non-nucleoside NS5B polymerase inhibitor	Nausea, pruritus, insomnia, diarrhea, asthenia	Oral	All oral- interferon-free therapy for the treatment of HCV-genotype 1. Designated by the FDA as a Breakthrough Therapy
Ceftolozane / tazobactam (Cubist Pharmaceuticals)	Cephalosporins (eg ceftazidime) and beta- lactamase inhibitors	Treatment of complicated urinary tract infections and complicated intra- abdominal infections caused by gram-negative bacteria	Ceftolozane: inhibition of penicillin- binding proteins; cephalosporin; Tazobactam: beta-lactamase inhibitor	Abdominal pain, nausea, headache, paresthesia, somnolence, vulvovaginal pruritus, constipation	Intravenous	Granted fast- track status as a Qualified Infectious Disease Product

Table 5. Supplemental applications filed by manufacturer: April 16, 2014 through May 15, 2014

Generic name	Brand name (Company)	comments
Paliperidone palmitate	<i>Invega Sustenna</i> (Janssen Pharmaceuticals)	Once-monthly injection for treatment of schizoaffective disorder as either monotherapy or adjunctive therapy
Simeprevir / sofosbuvir	(Janssen /Gilead Sciences)	Combination of a NS3/4A protease inhibitor and a nucleotide analog NS5B polymerase inhibitor to treatment patients infected with hepatitis C virus

Table 6. Significant labeling changes or “Dear Health Professional” letters related to safety^a

Generic name <i>Brand name</i> (Company)	Warning
Dabigatran <i>Pradaxa</i> (Boehringer Ingelheim)	Drug Safety Communication: Medicare patients comparing dabigatran to warfarin, for risk of ischemic or clot-related stroke, bleeding in the brain, major gastrointestinal (GI) bleeding, myocardial infarction (MI), and death. Among new users of blood-thinning drugs, dabigatran was associated with a lower risk of clot-related strokes, bleeding in the brain, and death than warfarin, but an increased risk of major gastrointestinal bleeding. The MI risk was similar for the 2 drugs. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm397179.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery
Epidural corticosteroid injections	Injection of corticosteroids into the epidural space may result in loss of vision, stroke, paralysis, and death. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm397179.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery
Eszopiclone <i>Lunesta</i> (Sunovion Pharmaceuticals)	Warning regarding the risk of next-day impairment of driving and other activities that require alertness. Recommended starting dose is being decreased to 1 mg at bedtime. http://www.fda.gov/Drugs/DrugSafety/ucm397260.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

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