Current FDA-Related Drug Information

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

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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 bakerdan@wsu.edu.

Table 1. New drugs approved by the US Food and Drug Administration (FDA): December 21, 2012 through January 17, 2013

Apixaban – Eliquis (Bristol Myers Squibb)

Comparative agents:	Anticoagulants, oral
Indication:	Reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation
Mechanism of action:	Factor Xa inhibitor
Common adverse effects:	Bleeding
Dosage form & strength:	Tablet; 2.5 and 5 mg
Product labeling:	http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202155s000lbl.pdf

Bedaquiline – Sirturo (Janssen)

Comparative agents:	Isoniazid
Indication:	Combination therapy in adults (≥ 18 years) with pulmonary multidrug-resistant tuberculosis. Reserve for use when an effective treatment regimen cannot otherwise be provided. It is not indicated for the treatment of latent, extrapulmonary, or drug-sensitive tuberculosis.
Mechanism of action:	Inhibits mycobacterial ATP (adenosine 5'-triphosphate) synthase, an enzyme that is essential for the generation of energy in <i>Mycobacterium tuberculosis</i> .
Common adverse effects:	Nausea, arthralgia, headache
Dosage form & strength:	Tablet; 100 mg
Product labeling:	http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/204384s000lbl.pdf

Budesonide – Uceris (Santarus)

Comparative agents:	Budesonide (Entocort EC)
Indication:	Induction of remission in patients with active, mild to moderate ulcerative colitis
Mechanism of action:	Corticosteroid – anti-inflammatory activity
Common adverse effects:	Headache, nausea, decreased blood cortisol, upper abdominal pain, fatigue, flatulence, abdominal distension, acne, urinary tract infection, arthralgia, and constipation
Dosage form & strength:	Extended-release tablet; 9 mg
Product labeling:	http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/203634s000lbl.pdf

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Table 1. New drugs approved by the US Food and Drug Administration (FDA): December 21, 2012 through January 17, 2013 (CONT.)

Crofelemer – Fulyzaq (Salix Pharmaceuticals)	
<i>Comparative agents:</i>	Loperamide
<i>Indication:</i>	Symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy
<i>Mechanism of action:</i>	Decreased chloride secretion and volume in the gastrointestinal tract through the inhibition of both the cyclic adenosine monophosphate (cAMP)-stimulated cystic fibrosis transmembrane conductance regulator (CFTR) chloride ion (Cl ⁻) channel and the calcium-activated Cl ⁻ channels at the luminal membrane of enterocytes.
<i>Common adverse effects:</i>	Upper respiratory tract infection, bronchitis, cough, flatulence, and increased bilirubin
<i>Dosage form & strength:</i>	Delayed release tablets; 125 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202292s000lbl.pdf
Influenza vaccine – Flublok (Protein Sciences Corporation)	
<i>Comparative agents:</i>	Influenza vaccines
<i>Indication:</i>	Active immunization, in persons 18 through 49 years of age, against disease caused by influenza virus subtypes A and type B contained in the vaccine
<i>Mechanism of action:</i>	Immune system activation
<i>Common adverse effects:</i>	Injection site reaction, pain at the injection site, headache, fatigue, myalgia
<i>Dosage form & strength:</i>	Injection; viral formula changes annually
<i>Product labeling:</i>	http://www.flublok.com/FlublokInsert.pdf
Loxapine – Adasuve (Alexza Pharm)	
<i>Comparative agents:</i>	Loxapine
<i>Indication:</i>	Acute treatment of agitation associated with schizophrenia or bipolar 1 disorder in adults
<i>Mechanism of action:</i>	Antagonism of central dopamine D2 and serotonin 5-HT2A receptors
<i>Common adverse effects:</i>	Dysgeusia, sedation, throat irritation
<i>Dosage form & strength:</i>	Inhalation powder; 10 mg
<i>Product labeling:</i>	www.adauve.com
Lomitapide – Juxtapid (Aegerion Pharmaceuticals)	
<i>Comparative agents:</i>	Statins
<i>Indication:</i>	Adjunct to a low-fat diet and other lipid-lowering treatments, including low-density lipoprotein (LDL) apheresis where available, to reduce LDL cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH)
<i>Mechanism of action:</i>	Binds and inhibits microsomal triglyceride transfer protein (MTP), which resides in the lumen of the endoplasmic reticulum, thereby preventing the assembly of apo B containing lipoproteins in enterocytes and hepatocytes
<i>Common adverse effects:</i>	Diarrhea, nausea, vomiting, dyspepsia, and abdominal pain
<i>Dosage form & strength:</i>	Capsule; 5, 10, and 20 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/203858s000lbl.pdf
Levonorgestrel – Skyla (Bayer HealthCare Pharmaceuticals)	
<i>Comparative agents:</i>	Intrauterine system
<i>Indication:</i>	Prevention of pregnancy
<i>Mechanism of action:</i>	Thickening of cervical mucus preventing passage of sperm into the uterus, inhibition of sperm capacitation or survival, and alteration of the endometrium
<i>Common adverse effects:</i>	Bleeding pattern alterations, vulvovaginitis, abdominal/pelvic pain, acne/seborrhea, ovarian cyst, and headache
<i>Dosage form & strength:</i>	T-shaped polyethylene frame with a steroid reservoir: levonorgestrel 13.5 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/203159s000lbl.pdf

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Table 1. New drugs approved by the US Food and Drug Administration (FDA): December 21, 2012 through January 17, 2013 (CONT.)

Teduglutide – Gattex (NPS Pharmaceuticals)	
<i>Comparative agents:</i>	None
<i>Indication:</i>	Treatment of adult patients with short bowel syndrome who are dependent on parenteral support
<i>Mechanism of action:</i>	Analog of naturally occurring human glucagon-like peptide-2 (GLP-2), a peptide secreted by L-cells of the distal intestine. GLP-2 is known to increase intestinal and portal blood flow and inhibit gastric acid secretion.
<i>Common adverse effects:</i>	Abdominal pain, injection site reactions, nausea, headaches, abdominal distension, upper respiratory tract infection
<i>Dosage form & strength:</i>	Injection SQ; 5 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/203441Orig1s000lbl.pdf

Table 2. New dosage forms and indications approved by the FDA: December 21, 2012 through January 17, 2013

Generic name	Brand name (Company)	Indication and comments
New dosage forms/strength/ route of administration		
Interferon beta-1a	<i>Rebif</i> (EMD Serono)	Approval of the new prefilled syringe that is designed to make the use of the product easier for patients
New indications		
Anakinra	<i>Kineret</i> (Biovitrum AB)	Treatment of neonatal-onset multisystem inflammatory disease (NOMID)
Oseltamivir	<i>Tamiflu</i> (Roche)	Use for the treatment of acute, uncomplicated influenza expanded to include patients 2 weeks of age and older who have been symptomatic for no more than 2 days
Varicella zoster immune globulin	<i>Varizig</i> (Cangene Corporation)	Reducing the severity of chickenpox (varicella zoster virus) infections in high-risk individuals when given within 4 days after exposure

Table 3. Agents pending FDA approval: December 21, 2012 through January 17, 2013

Generic name	Brand name (Company)	Indication and comments
Delayed decision by the FDA		
RP103	<i>Procysbi</i> (Raptor Pharmaceutical)	Treatment of nephropathic cystinosis
Glycerol phenylbutyrate	<i>Ravicti</i> (Hyperion Therapeutics)	Treatment of urea cycle disorders
Recommended for approval by an FDA advisory panel		
Canagliflozin	<i>Invokana</i> (Janssen)	Recommended for approval (10:5) for the treatment of adults with type 2 diabetes

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Table 3. Agents pending FDA approval: December 21, 2012 through January 17, 2013 (CONT.)

Recommended for NON-approval by an FDA advisory panel		
Rintatolimod	<i>Ampligen</i> (Hemispherx Biopharma)	Treatment of chronic fatigue syndrome; insufficient efficacy and safety data to support approval
Agents scheduled for review by an FDA advisory panel		
Fluticasone furoate / vilanterol	<i>Breo Ellipta</i> (GlaxoSmithKline)	Long-term maintenance treatment of airflow obstruction and to reduce exacerbations in patients with chronic obstructive pulmonary disease
Gabapentin	(Depomed)	Treatment of moderate to severe vasomotor symptoms due to menopause

Table 4. New drug / biologics license applications filed by manufacturer: December 21, 2012 through January 17, 2013

Generic name <i>Brand name</i> (Company)	Comparative agents	Indication	Mechanism of action	Common adverse effects	Dosage form or route	Comments
Albiglutide (GlaxoSmithKline)	GLP-1s (eg, exenatide, liraglutide)	Treatment of adult patients with type 2 diabetes	Glucagon-like peptide-1 (GLP-1) receptor agonist	Nausea, vomiting, flatulence, abdominal pain, headache, dizziness	Injection	Once weekly administration

Table 5. Supplemental applications filed by manufacturer: December 21, 2012 through January 17, 2013

Generic name	<i>Brand name</i> (Company)	Comments
Alvimopan	<i>Entereg</i> (Cubist Pharmaceuticals)	Accelerate gastrointestinal recovery following any surgery that includes a bowel resection with primary anastomosis.
Erlotinib	<i>Tarceva</i> (Astellas Pharma)	First-line use in patients with locally advanced or metastatic non-small-cell lung cancer whose tumors have epidermal growth factor receptor activating mutations
Ferumoxytol	<i>Feraheme</i> (AMAG Pharma)	Expanded for use in all patients with iron deficiency anemia who have failed or cannot tolerate oral iron treatment
Natalizumab	<i>Tysabri</i> (Biogen Idec)	First-line use for patients living with relapsing forms of multiple sclerosis who have tested negative for antibodies to the JC virus

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

Generic name <i>Brand name</i> (Company)	Warning
Abiraterone acetate <i>Zytiga</i> (Janssen Biotech)	<p>CONTRAINDICATIONS</p> <ul style="list-style-type: none"> • Can cause fetal harm when administered to a pregnant woman; drug is not indicated for use in women. <p>WARNINGS AND PRECAUTIONS</p> <ul style="list-style-type: none"> • May cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition • Adrenocortical insufficiency may occur during treatment • Grade 3 or 4 ALT or AST increases (at least 5x ULN) occurred in ~4% of patients treated with abiraterone, most of these liver function test changes occurred during the first 3 months of treatment. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm314608.htm</p>
Citalopram Desvenlafaxine Escitalopram Paroxetine Sertraline Trimipramine Venlafaxine Vilazodone (various)	<p>CLASS WARNING: Risk of serotonin toxicity associated with co-administration with linezolid and methylene blue.</p>
Dabigatran etexilate <i>Pradaxa</i> (Boehringer Ingelheim)	<p>Use in patients with mechanical prosthetic heart value added as a contraindication. Risk of thromboembolic and bleeding events in patients with prosthetic heart values was added to the Warnings and Precautions section.</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm335508.htm</p>
Peginesatide <i>Omontys</i> (Affymax)	<p>Serious allergic reactions added as a contraindication for use. Information regarding the risk of serious allergic reactions added to the Warnings and Precautions section. Reactions have included anaphylactic reactions, hypotension, bronchospasm, angioedema, and generalized pruritus.</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm334681.htm</p>
Zolpidem Various (various)	<p>To decrease the risk of next-morning impairment, the dose of zolpidem is being reduced:</p> <p>Women: Decreased from 10 mg to 5 mg for immediate-release products and from 12.5 mg to 6.25 mg for extended-release products.</p> <p>Men: Recommendation for use of lower doses similar to those recommended for women.</p> <p>Middle-of-the night awakening products (eg, <i>Intermezzo</i>): no change in dose</p>

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