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 danial.baker@wsu.edu.

Table 1. New drugs approved by the US Food and Drug Administration: August 19, 2015 through September 25, 2015

Cariprazine – Vraylar (Forest Labs)	
<i>Comparative agents:</i>	Atypical antipsychotics
<i>Indication:</i>	Treatment of schizophrenia; acute treatment of manic or mixed episodes associated with bipolar I disorder
<i>Mechanism of action:</i>	Unknown; partial agonist activity at central dopamine D2 and serotonin 5-HT1A receptors and antagonist activity at serotonin 5-HT2A receptors
<i>Common adverse effects:</i>	Extrapyramidal symptoms, akathisia, dyspepsia, vomiting, somnolence, and restlessness
<i>Dosage form & strength:</i>	Capsules; 1.5 mg, 3 mg, 4.5 mg, and 6 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/204370lbl.pdf
Evolocumab – Repatha (Amgen)	
<i>Comparative agents:</i>	Alirocumab
<i>Indication:</i>	Adjunct to diet and maximally tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C) and in patients with homozygous familial hypercholesterolemia (HoFH) who are receiving other LDL-lowering therapies (eg, statins, ezetimibe, LDL apheresis) but still require additional lowering of LDL-C.
<i>Mechanism of action:</i>	Human monoclonal IgG2 directed against human proprotein convertase subtilisin kexin 9 (PCSK9), also known as a PCSK9 inhibitor
<i>Common adverse effects:</i>	Nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions
<i>Dosage form & strength:</i>	Injection; 140 mg/mL single-use prefilled syringe and single-use prefilled SureClick autoinjector
<i>Product labeling:</i>	http://pi.amgen.com/united_states/repatha/repatha_pi_hcp_english.pdf

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Table 1. New drugs approved by the US Food and Drug Administration: August 19, 2015 through September 25, 2015 (CONT.)

Flibanserin – Addyi (Sprout Pharmaceuticals)	
<i>Comparative agents:</i>	None
<i>Indication:</i>	Treatment of premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD) as characterized by low sexual desire that causes marked distress or interpersonal difficulty and is <u>not</u> due to co-existing medical or psychiatric conditions, problems within the relationship, or effects of a medication or other drug substance.
<i>Mechanism of action:</i>	Unknown; serotonin 5-HT _{1A} agonist and 5HT _{2A} antagonist
<i>Common adverse effects:</i>	Dizziness, somnolence, nausea, fatigue, insomnia, and dry mouth
<i>Dosage form & strength:</i>	Tablet, 100 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022526lbl.pdf
Insulin degludec – Tresiba (Novo Nordisk)	
<i>Comparative agents:</i>	Long-acting insulins
<i>Indication:</i>	Improvement in blood glucose control in adults with diabetes mellitus
<i>Mechanism of action:</i>	Insulin – glucose level modulation
<i>Common adverse effects:</i>	Hypoglycemia, allergic reactions, injection site reactions, pitting at the injection site (lipodystrophy), itching, rash, edema, and weight gain
<i>Dosage form & strength:</i>	Injection; 100 units/mL and 200 units/mL
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/203314lbl.pdf
Insulin degludec/Insulin aspart – Ryzodeg 70/30 (Novo Nordisk)	
<i>Comparative agents:</i>	Long-acting insulin/rapid acting insulin
<i>Indication:</i>	Improvement in blood glucose control in adults with diabetes mellitus
<i>Mechanism of action:</i>	Insulin – glucose level modulation
<i>Common adverse effects:</i>	Injection site reactions, hypoglycemia, allergic reactions, pitting at the injection site (lipodystrophy), itching, rash, edema, and weight gain
<i>Dosage form & strength:</i>	Injection; 70/30 (insulin degludec and insulin aspart) 100 units/mL
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/203313lbl.pdf
Recombinant antihemophilic factor (blood factor VIII) – Nuwiq (Octapharma)	
<i>Comparative agents:</i>	Other antihemophilic factors
<i>Indication:</i>	Adults and children with hemophilia A for on-demand treatment and control of bleeding episodes, perioperative management of bleeding, or routine prophylaxis to reduce the frequency of bleeding episodes
<i>Mechanism of action:</i>	Replacement of missing or deficient coagulation Factor VIII
<i>Common adverse effects:</i>	Paresthesia, headache, injection site reactions, non-neutralizing anti-Factor VIII antibody formation, back pain, vertigo, and dry mouth
<i>Dosage form & strength:</i>	Vials; labeled with actual amount of Factor VIII potency in international units
<i>Product labeling:</i>	http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/UCM461328.pdf

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Table 1. New drugs approved by the US Food and Drug Administration: August 19, 2015 through September 25, 2015 (CONT.)

Rolapitant – Varubi (Tesarco)	
<i>Comparative agents:</i>	Aprepitant, fosaprepitant, netupitant/palonosetron
<i>Indication:</i>	Combination therapy with other antiemetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.
<i>Mechanism of action:</i>	Substance P/neurokinin 1 (NK1) receptor antagonist
<i>Common adverse effects:</i>	Mainly the adverse reactions related to the chemotherapy the patient is receiving; neutropenia, hiccups, decreased appetite, dizziness
<i>Dosage form & strength:</i>	Tablet; 90 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206500s000lbl.pdf
Trifluridine/tipiracil – Lonsurf (Taiho Oncology)	
<i>Comparative agents:</i>	None
<i>Indication:</i>	Treatment of patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy.
<i>Mechanism of action:</i>	Trifluridine is a nucleoside metabolic inhibitor and tipiracil is a thymidine phosphorylase inhibitor.
<i>Common adverse effects:</i>	Anemia, neutropenia, fatigue, nausea, thrombocytopenia, decreased appetite, diarrhea, vomiting, abdominal pain, pyrexia
<i>Dosage form & strength:</i>	Tablets; 15 mg/6.14 mg, 20 mg/8.19 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207981s000lbl.pdf
Uridine triacetate – Xuriden (Wellstat Therapeutics)	
<i>Comparative agents:</i>	None
<i>Indication:</i>	Uridine replacement indicated for the treatment of hereditary orotic aciduria
<i>Mechanism of action:</i>	Pyrimidine analog used for uridine replacement
<i>Common adverse effects:</i>	None
<i>Dosage form & strength:</i>	Packets; 2 g
<i>Product labeling:</i>	http://www.xuriden.com/fpi.pdf

Table 2. New dosage forms and indications approved by the FDA: August 19, 2015 through September 25, 2015

Generic name	Brand name (Company)	Indication and comments
New dosage forms/strength/route of administration		
Aspirin	<i>Durlaza</i> (New Haven Pharma)	24-hour extended release aspirin (162.5 mg) for secondary prevention in patients with a high risk of cardiovascular events, including stroke and heart attack
Empagliflozin/metformin	<i>Synjardy</i> (Boehringer Ingelheim)	Combination tablet with 2 previously approved drugs for adjuvant therapy with diet and exercise to treatment patients with type 2 diabetes mellitus
Ticagrelor	<i>Brilinta</i> (AstraZeneca)	60 mg twice daily, along with aspirin, for patient with a history of heart attack beyond the first year

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Table 2. New dosage forms and indications approved by the FDA: August 19, 2015 through September 25, 2015 (CONT.)

New indications		
Adalimumab	<i>Humira</i> (AbbVie)	Treatment of moderate to severe hidradenitis suppurativa (HS; Hurley stage II and Hurley stage III disease)
Brentuximab vedotin	<i>Adcetris</i> (Seattle Genetics)	Treatment of patients with classical Hodgkin lymphoma at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation
Cysteamine bitartrate	<i>Procysbi</i> (Raptor Pharmaceutical)	Used to treat children 2 to 6 years of age with nephropathic cystinosis
Eltrombopag	<i>Promacta</i> (Novartis)	Treatment of pediatric patients 1 year and older with chronic immune thrombocytopenia who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
Eslicarbazepine	<i>Aptiom</i> (Sunovion Pharms)	Monotherapy treatment of partial-onset seizures in adults
Oxycodone	<i>OxyContin</i> (Purdue)	Patients aged 11 to 16 years
Tiotropium	<i>Spiriva Respimat</i> (Boehringer Ingelheim)	Long-term, once-daily maintenance treatment of asthma in patients 12 years of age and older

Table 3. Agents pending FDA approval: August 19, 2015 through September 25, 2015

Generic name	Brand name (Company)	Indication and comments
Agents scheduled for review by an FDA advisory panel		
Enclomiphene citrate	(Repros Therapeutics)	Treatment of secondary hypogonadism in fertile men, younger than 60 years of age with a body mass index over 25 kg/m ² . Meeting scheduled for November 3, 2015.
Lesinurad	(Ardea Biosciences)	Adjunctive therapy with xanthine oxidase inhibitor for the treatment of hyperuricemia associated with gout. Meeting scheduled for October 23, 2015.

Table 4. Significant labeling changes or “Dear Health Professional” letters related to safety^a

Generic name Brand name (Company)	Warning
ACE inhibitors and mTOR inhibitor coadministration	Increased risk for angioedema http://fda.gov/Safety/MedWatch/SafetyInformation/ucm461227.htm
Alogliptin, Linagliptin, Sitagliptin, Saxagliptin (DPP-4 inhibitors) (Various)	Treatment with these drugs has been associated with joint pain that can be severe and disabling. If the DPP-4 inhibitor is suspected to be the cause of the joint pain, discontinuation of therapy should be considered. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm460238.htm

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Table 4. Significant labeling changes or “Dear Health Professional” letters related to safety^a (CONT.)

Bendamustine hydrochloride <i>Treanda</i> (Teva)	Use in closed system transfer devices (CSTDs), adapters, and syringes containing polycarbonate or acrylonitrile-butadiene-styrene (ABS) is not recommended. The drug should only be used with compatible devices with which it has been shown to be compatible. http://www.fda.gov/Drugs/DrugSafety/ucm437469.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery
Bismuth subsalicylate/metronidazole/tetracycline <i>Helidac</i> (Prometheus Labs)	<p>WARNINGS</p> <p>Potential for Carcinogenicity</p> <ul style="list-style-type: none"> Metronidazole has been shown to be carcinogenic in mice and rats. It is unknown whether metronidazole is associated with carcinogenicity in humans. <p>Cutaneous Reactions</p> <ul style="list-style-type: none"> Skin and subcutaneous disorders including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis, and DRESS syndrome (drug rash with eosinophilia and systemic symptoms) have been reported. Discontinue treatment at the first evidence of a cutaneous reaction. <p>PRECAUTIONS</p> <p>Increased Plasma Concentrations in Patients with Hepatic Impairment</p> <ul style="list-style-type: none"> Patients with hepatic impairment metabolize metronidazole slowly, with resultant accumulation of metronidazole in the plasma. Use <i>Helidac</i> therapy with caution in patients with mild to moderate hepatic impairment. <i>Helidac</i> therapy may not be appropriate for patients with severe hepatic impairment (Child-Pugh C). <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm310885.htm</p>
Brentuximab vedotin <i>Adcetris</i> (Seattle Genetics)	<p>WARNINGS AND PRECAUTIONS</p> <p>Pulmonary Toxicity</p> <ul style="list-style-type: none"> Events of noninfectious pulmonary toxicity including pneumonitis, interstitial lung disease, and acute respiratory distress syndrome (ARDS), some with fatal outcomes, have been reported. Interruption of therapy may be necessary. <p>ADVERSE REACTIONS</p> <p>Postmarketing</p> <ul style="list-style-type: none"> Respiratory, thoracic, and mediastinal disorders: Noninfectious pulmonary toxicity including pneumonitis, interstitial lung disease, and ARDS (some with fatal outcomes). <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm426241.htm</p>
Canagliflozin <i>Invokana</i> (Janssen Pharms)	Strengthened the warning for the type 2 diabetes medicine canagliflozin products related to the increased risk of bone fractures. http://www.fda.gov/Drugs/DrugSafety/ucm461449.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery
Ceftazidime/avibactam <i>Avycaz</i> (Cereza)	Risk for dosing errors with the intravenous antibacterial drug <i>Avycaz</i> (ceftazidime and avibactam) due to confusion about the drug strength displayed on the vial and carton labels. To prevent further medication errors, the label will be revised to indicate that each vial contains <i>Avycaz</i> 2.5 g, equivalent to ceftazidime 2 g and avibactam 0.5 g. http://www.fda.gov/Drugs/DrugSafety/ucm463248.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery
Clozapine (Various)	Changes to the requirements for monitoring, prescribing, dispensing, and receiving the schizophrenia medicine clozapine because of the risk of neutropenia. There are 2 parts to the changes in the requirements for treating patients with clozapine; clarification and enhanced the prescribing information for clozapine that explains how to monitor patients for neutropenia and manage clozapine treatment and new, shared risk evaluation and mitigation strategy (REMS) called the Clozapine REMS Program. http://www.fda.gov/Drugs/DrugSafety/ucm461853.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

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Table 4. Significant labeling changes or “Dear Health Professional” letters related to safety^a (CONT.)

Dasatinib <i>Sprycel</i> (Bristol-Myers Squibb)	<p>WARNINGS AND PRECAUTIONS</p> <p>Myelosuppression</p> <ul style="list-style-type: none"> In patients with chronic phase CML, perform complete blood counts (CBCs) every 2 weeks for 12 weeks, then every 3 months thereafter, or as clinically indicated. In patients with advanced phase CML or Ph+ ALL, perform CBCs weekly for the first 2 months and then monthly thereafter, or as clinically indicated. <p>Fluid Retention</p> <ul style="list-style-type: none"> <i>Sprycel</i> may cause fluid retention. Evaluate patients who develop symptoms of pleural effusion or other fluid retention, such as new or worsened dyspnea on exertion or at rest, pleuritic chest pain, or dry cough promptly with a chest x-ray or additional diagnostic imaging as appropriate. Fluid retention events were typically managed by supportive care measures that may include diuretics or short courses of steroids. Severe pleural effusion may require thoracentesis and oxygen therapy. Consider dose reduction or treatment interruption. <p>Severe Dermatologic Reactions</p> <ul style="list-style-type: none"> Cases of severe mucocutaneous dermatologic reactions, including SJS and erythema multiforme, have been reported. Discontinue permanently in patients who experience a severe mucocutaneous reaction during treatment if no other etiology can be identified. <p>ADVERSE REACTIONS</p> <p>Postmarketing Experience</p> <ul style="list-style-type: none"> Skin and subcutaneous tissue disorders: SJS <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm223728.htm</p>
Enzalutamide <i>Xtandi</i> (Astellas)	<p>WARNINGS AND PRECAUTIONS</p> <p>Posterior Reversible Encephalopathy Syndrome (PRES)</p> <ul style="list-style-type: none"> PRES has been reported. PRES is a neurological disorder, which can present with rapidly evolving symptoms including seizure, headache, lethargy, confusion, blindness, and other visual and neurological disturbances, with or without associated hypertension. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm460724.htm</p>
Etonogestrel implants <i>Implanon & Nexplanon</i> (various)	<p>WARNINGS and PRECAUTIONS</p> <p>In Situ Broken or Bent Implant</p> <ul style="list-style-type: none"> There have been reports of broken or bent implants while in the patient's arm. Based on in vitro data, when an implant is broken or bent, the release rate of etonogestrel may be slightly increased. When an implant is removed, it is important to remove it in its entirety. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm400440.htm</p>
Fingolimod <i>Gilenya</i> (Novartis)	<p>WARNINGS AND PRECAUTIONS</p> <p>Progressive Multifocal Leukoencephalopathy</p> <ul style="list-style-type: none"> A case of progressive multifocal leukoencephalopathy (PML) and a case of probable PML occurred in patients with multiple sclerosis (MS) who received <i>Gilenya</i> in the postmarketing setting. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm266123.htm</p>
Ingenol mebutate <i>Picato</i> (LEO Pharma)	<p>Reports of severe allergic reactions and herpes zoster (shingles) associated with the use of this product. Some of these cases may have been associated with the patient applying the product to skin areas larger than recommended or for prolonged periods of time.</p> <p>http://www.fda.gov/Drugs/DrugSafety/ucm459142.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery</p>

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Table 4. Significant labeling changes or “Dear Health Professional” letters related to safety^a (CONT.)

Interferon gamma-1b <i>Actimmune</i> (Vidara Therapeutics Research)	<p>WARNINGS AND PRECAUTIONS</p> <p>Hypersensitivity Reactions</p> <ul style="list-style-type: none"> Isolated cases of acute serious hypersensitivity reactions and transient cutaneous rashes have been observed. If such an acute reaction develops, the drug should be discontinued immediately and appropriate medical therapy instituted. If the transient cutaneous rashes occur, treatment interruption may be necessary. <p>Renal Toxicity</p> <ul style="list-style-type: none"> Monitor renal function regularly in patients with severe renal insufficiency because the possibility exists that accumulation of interferon gamma-1b may occur. Renal toxicity has been reported in some patients. <p>Allergic Reactions to Natural Rubber</p> <ul style="list-style-type: none"> The stopper of the glass vial for <i>Actimmune</i> contains natural rubber (a derivative of latex), which may cause allergic reactions. <p>ADVERSE REACTIONS</p> <p>Immunogenicity</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm461751.htm</p>
Methoxy polyethylene glycol-epoetin beta <i>Mircera</i> (Roche)	<p>WARNINGS AND PRECAUTIONS</p> <p>Serious Allergic Reactions</p> <ul style="list-style-type: none"> Serious allergic reactions, including SJS/toxic epidermal necrolysis, have been reported. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm423232.htm</p>
Methylphenidate transdermal system <i>Daytrana</i> (Noven Pharms)	<p>WARNINGS AND PRECAUTIONS</p> <p>Chemical Leukoderma</p> <ul style="list-style-type: none"> May result in a persistent loss of skin pigmentation at and around the application site. Loss of pigmentation, in some cases, has been reported at other sites distant from the application site. Chemical leukoderma can mimic the appearance of vitiligo, particularly when the loss of skin pigmentation involves areas distant from the application site. Individuals with a history of vitiligo and/or a family history of vitiligo may be more at risk. Skin depigmentation may persist even after use of <i>Daytrana</i> is discontinued. Discontinue the <i>Daytrana</i> patch in patients with chemical leukoderma. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm460720.htm</p>
Mirabegron <i>Myrbetriq</i> (Apgdi)	<p>WARNINGS AND PRECAUTIONS</p> <p>Angioedema</p> <ul style="list-style-type: none"> Angioedema of the face, lips, tongue, and/or larynx has been reported with <i>Myrbetriq</i>. If involvement of the tongue, hypopharynx, or larynx occurs, promptly discontinue <i>Myrbetriq</i> and initiate appropriate therapy and/or measures necessary to ensure a patent airway. <p>ADVERSE REACTIONS</p> <p>Postmarketing Experience</p> <ul style="list-style-type: none"> Skin and subcutaneous tissue: Angioedema of the face, lips, tongue, and larynx, with or without respiratory symptoms. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm461229.htm</p>
OnabotulinumtoxinA <i>Botox</i> (Allergan)	<p>WARNINGS AND PRECAUTIONS</p> <p>Serious Adverse Reactions with Unapproved Use</p> <ul style="list-style-type: none"> Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported in patients who received <i>Botox</i> injections for unapproved uses. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm460726.htm</p>

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Table 4. Significant labeling changes or “Dear Health Professional” letters related to safety^a (CONT.)

Orlistat <i>Xenical</i> (Roche)	<p>ADVERSE REACTIONS</p> <p>Rare cases of leukocytoclastic vasculitis have been reported. Clinical signs include palpable purpura, maculopapular lesions, or bullous eruption.</p> <p>DRUG INTERACTIONS</p> <p>Amiodarone</p> <ul style="list-style-type: none"> Decreased levels of amiodarone and its metabolite, desethylamiodarone, may occur with concurrent therapy. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm215504.htm</p>
Ribavirin <i>Copegus</i> (Roche)	<p>WARNINGS AND PRECAUTIONS</p> <p>Impact on Growth in Pediatric Patients</p> <ul style="list-style-type: none"> Decreases in weight for age z-score and height for age z-score up to 48 weeks of therapy compared with baseline were observed. <p>ADVERSE REACTIONS</p> <p>Growth Inhibition in Pediatric Subjects</p> <ul style="list-style-type: none"> Pediatric subjects treated with PEGASYS plus ribavirin combination therapy showed a delay in weight and height increases with up to 48 weeks of therapy compared with baseline. At the end of 2 years follow-up after treatment, most subjects had returned to baseline normative curve percentiles for weight and height. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm218877.htm</p>
Sofosbuvir <i>Sovaldi</i> (Gilead Sciences)	<p>WARNINGS AND PRECAUTIONS</p> <p>Risks Associated with Combination Treatment</p> <ul style="list-style-type: none"> Use in combination with other antiviral drugs for treatment of hepatitis C virus (HCV) infection. Warnings and Precautions related to these drugs also apply to their use in <i>Sovaldi</i> combination treatment. <p>Related Products Not Recommended</p> <ul style="list-style-type: none"> The use of <i>Sovaldi</i> with other products containing sofosbuvir is not recommended. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm441356.htm</p>
Thalidomide <i>Thalomid</i> (Celgene)	<p>WARNINGS AND PRECAUTIONS</p> <p>Thrombocytopenia</p> <ul style="list-style-type: none"> Thrombocytopenia, including Grade 3 or 4 occurrences, has been reported. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm402899.htm</p>
Vemurafenib <i>Zelboraf</i> (Roche)	<p>WARNINGS AND PRECAUTIONS</p> <p>Radiation Sensitization and Radiation Recall</p> <ul style="list-style-type: none"> Radiation sensitization and recall, in some cases severe, involving cutaneous and visceral organs have been reported. <p>ADVERSE REACTIONS</p> <p>Postmarketing Experience</p> <ul style="list-style-type: none"> Injury, poisoning and procedural complications: Radiation sensitization and recall Gastrointestinal disorders: Pancreatitis <p>DRUG INTERACTIONS</p> <p>Effect of Vemurafenib on P-gp Substrates</p> <ul style="list-style-type: none"> Coadministration of <i>Zelboraf</i> with digoxin, a sensitive P-glycoprotein (P-gp) substrate, increased digoxin systemic exposure by 1.8-fold. Avoid concurrent use of P-gp substrates known to have narrow therapeutic indices. If use of these medications is unavoidable, consider dose reduction of P-gp substrates with narrow therapeutic indices. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm364374.htm</p>
Ziprasidone <i>Geodon</i> (Pfizer)	<p>WARNINGS AND PRECAUTIONS</p> <p>Severe Cutaneous Adverse Reactions</p> <ul style="list-style-type: none"> Other severe cutaneous adverse reactions, such as SJS, have been reported with ziprasidone exposure. Discontinue ziprasidone if severe cutaneous adverse reactions are suspected. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm346729.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. ■