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 (FDA): August 16, 2014 through September 15, 2014

Eliglustat – Cerdelga (Genzyme)	
<i>Comparative agents:</i>	Imiglucerase, Velaglucerase, Taliglucerase
<i>Indication:</i>	Long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test
<i>Mechanism of action:</i>	Specific inhibitor of glucosylceramide synthase
<i>Common adverse effects:</i>	Fatigue, headache, nausea, diarrhea, back pain, pain in extremities, upper abdominal pain
<i>Dosage form & strength:</i>	Capsules; 84 mg
<i>Product labeling:</i>	http://www.cerdelga.com/pdf/cerdelga_prescribing_information.pdf
Ferric citrate – (Keryx Biopharmaceuticals)	
<i>Comparative agents:</i>	Calcium acetate, calcium carbonate, lanthanum carbonate, sevelamer hydrochloride, sevelamer carbonate, sucroferric oxyhydroxide
<i>Indication:</i>	Control of serum phosphorus levels in patients with chronic kidney disease on dialysis
<i>Mechanism of action:</i>	Iron-based phosphate binder complex
<i>Common adverse effects:</i>	Diarrhea, discolored feces, constipation, nausea, and vomiting
<i>Dosage form & strength:</i>	Oral; 210 mg ferric iron (equivalent to 1 g ferric citrate)
<i>Product labeling:</i>	http://keryx.com/wp-content/uploads/Keryx_FerricCitrate_PI.pdf
Fluticasone furoate – Arnuity Ellipta (GlaxoSmithKline)	
<i>Comparative agents:</i>	Fluticasone propionate
<i>Indication:</i>	Maintenance treatment of asthma as prophylactic therapy in patients aged 12 years and older
<i>Mechanism of action:</i>	Corticosteroid; anti-inflammatory activity
<i>Common adverse effects:</i>	Upper respiratory tract infection, nasopharyngitis, headache, and bronchitis
<i>Dosage form & strength:</i>	Inhalation powder; 100 mcg, 200 mcg
<i>Product labeling:</i>	https://www.gsksource.com/gskprm/htdocs/documents/ARNUITY-ELLIPTA-PI-PIL.PDF

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Table 1. New drugs approved by the US Food and Drug Administration (FDA): August 16, 2014 through September 15, 2014 (CONT.)

Naltrexone HCl & Bupropion HCl – <i>Contrave</i> (Orexigen Therapeutics)	
<i>Comparative agents:</i>	Individual ingredients
<i>Indication:</i>	Adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of: 30 kg/m ² or greater (obese) or 27 kg/m ² or greater (overweight) in the presence of at least one weight-related comorbidity (eg, hypertension, type 2 diabetes mellitus, or dyslipidemia)
<i>Mechanism of action:</i>	Opioid antagonist; aminoketone antidepressant; mechanism for weight control unknown, but may be related to activity in the hypothalamus (appetite regulatory center) and the mesolimbic dopamine circuit (reward system)
<i>Common adverse effects:</i>	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, and diarrhea
<i>Dosage form & strength:</i>	Extended-release tablet; naltrexone 8 mg/bupropion HCl 90 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/200063s000lbl.pdf
Peginterferon beta-1A – <i>Plegridy</i> (Biogen IDEC)	
<i>Comparative agents:</i>	Interferon beta 1-A
<i>Indication:</i>	Treatment of patients with relapsing forms of multiple sclerosis
<i>Mechanism of action:</i>	Unknown
<i>Common adverse effects:</i>	Injection site erythema, influenza-like illness, pyrexia, headache, myalgia, chills, injection site pain, asthenia, injection site pruritus, and arthralgia
<i>Dosage form & strength:</i>	Injection – single-dose prefilled syringe; 63 mcg/0.5 mL, 94 mcg/0.5 mL, 125 mcg/0.5 mL
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125499s000lbl.pdf

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

Generic name	Brand name (Company)	Indication and comments
New dosage forms/ strength/route of administration		
Abacavir, dolutegravir, and lamivudine	<i>Triumeq</i> (ViiV HealthCare)	Treatment of HIV-1 infection with a once-daily, single-tablet regimen that contains 600 mg of abacavir (nucleoside analogue reverse transcriptase inhibitor), 50 mg of dolutegravir (integrase strand transfer inhibitor), and 300 mg of lamivudine (nucleoside analogue reverse transcriptase inhibitor)
New indications		
Apixaban	<i>Eliquis</i> (Bristol-Myers Squibb)	Treatment of deep vein thrombosis and pulmonary emboli and reduction of risk of recurrent deep vein thrombosis and pulmonary emboli following initial therapy
Diclofenac	<i>Zorvolex</i> (Iroko Pharmaceuticals)	Management of osteoarthritis pain
Eltrombopag	<i>Promacta</i> (GlaxoSmithKline)	Treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy

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Table 2. New dosage forms and indications approved by the FDA: August 16, 2014 through September 15, 2014 (CONT.)

Generic name	Brand name (Company)	Indication and comments
Enalapril maleate powder for oral solution	<i>Epaned</i> (Silvergate Pharmaceuticals)	Previously approved only for the treatment of hypertension; indication expanded to include treatment of symptomatic heart failure and treatment of asymptomatic left ventricular dysfunction
Enzalutamide	<i>Xtandi</i> (Medivation/Astellas Pharma)	Advanced prostate cancer in men who have not yet received chemotherapy
Lacosamide	<i>Vimpat</i> (UCB)	Monotherapy for the treatment of partial-onset seizures in patients with epilepsy ages 17 years and older

Table 3. Agents pending FDA approval: August 16, 2014 through September 15, 2014

Generic name	Brand name (Company)	Indication and comments
Recommended for approval by an FDA advisory panel		
Aspirin/statin/antihypertensive		Potential for a fixed-combination antihypertensive, aspirin, and statin to reduce the risk of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke in patients with a history of cardiovascular disease (secondary prevention). Committee agreed with the concept to help improvement adherence, but concerns were expressed regarding the ability to achieve recommended target goal for lipid levels and blood pressure.
Recommended for NON-approval by an FDA advisory panel		
Nebivolol/valsartan	(Forest Laboratories)	Fixed combination (5/160 mg, 10/160 mg, 10/320 mg, and 20/320 mg) for the treatment of hypertension. The committee vote was 6 to 4 recommending against approval.
Agents scheduled for review by an FDA advisory panel		
Secukinumab	(Novartis)	Treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy
Testosterone undecanoate, oral	(Clarus Therapeutics)	Testosterone 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)
Varenicline	<i>Chantix</i> (Pfizer)	Evaluation of the risk of serious neuropsychiatric adverse events and options for addressing this risk

Table 4. New drug/biologics license applications filed by manufacturer: August 16, 2014 through September 15, 2014

Generic name <i>Brand name</i> (Company)	Comparative agents	Indication	Mechanism of action	Common adverse effects	Dosage form or route	Comments
Palbociclib (Pfizer)	None	Treatment of postmenopausal women with estrogen receptor positive (ER+), human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer who have not received previous systemic treatment for their advanced disease. Used in combination with letrozole.	Selective cyclin-dependent kinases (CDKs) 4 and 6 inhibitor; results in improvement in cell cycle control and blocks tumor cell proliferation	Neutropenia, leukopenia, fatigue, and anemia	Oral	Classified as breakthrough therapy by the FDA
Rolapitant (TESARO)	Aprepitant	Prevention of chemotherapy-induced nausea and vomiting	Neurokinin-1 (NK-1) receptor antagonist	Fatigue, alopecia, and constipation	Oral and intravenous	

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

Generic name <i>Brand name</i> (Company)	Warning
Adenosine <i>Adenoscan injection</i> (Astellas)	<p>WARNINGS AND PRECAUTIONS</p> <ul style="list-style-type: none"> Cerebrovascular accident hemorrhagic and ischemic cerebrovascular accidents have occurred. Hemodynamic effects of <i>Adenoscan</i> including hypotension or hypertension can be associated with these adverse reactions. <p>Seizures</p> <ul style="list-style-type: none"> New-onset or recurrence of convulsive seizures has occurred following <i>Adenoscan</i>. Some seizures are prolonged and require emergent anticonvulsive management. Aminophylline may increase the risk of seizures associated with <i>Adenoscan</i>. Methylxanthine use is not recommended in patients who experience seizures in association with <i>Adenoscan</i> administration. <p>Hypersensitivity</p> <ul style="list-style-type: none"> Dyspnea, throat tightness, flushing, erythema, rash, and chest discomfort have occurred. Symptomatic treatment may be required. Have personnel and appropriate treatment available. Resuscitative measures may be necessary if symptoms progress. <p>ADVERSE REACTIONS</p> <ul style="list-style-type: none"> Cerebrovascular accident; seizures; and hypersensitivity <p>USE IN SPECIFIC POPULATIONS</p> <p>Nursing Mothers</p> <ul style="list-style-type: none"> It is not known whether <i>Adenoscan</i> is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions from <i>Adenoscan</i> in nursing infants, the decision to interrupt nursing after administration of <i>Adenoscan</i> or not to administer <i>Adenoscan</i> should take into account the importance of the drug to the mother. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm246725.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
Almotriptan malate <i>Axert</i> (Janssen Pharmaceuticals)	<p>WARNINGS AND PRECAUTIONS</p> <p>Medication Overuse Headache</p> <ul style="list-style-type: none"> Overuse of acute migraine drugs (eg, ergotamine, triptans, opioids, or combination of these drugs for 10 or more days per month) may lead to exacerbation of headache (medication overuse headache). Medication overuse headache may present as migraine-like daily headaches or as a marked increase in frequency of migraine attacks. Detoxification of patients, including withdrawal of the overused drugs, and treatment of withdrawal symptoms (which often includes a transient worsening of headache) may be necessary. <p>ADVERSE REACTIONS</p> <p>Postmarketing Experience</p> <ul style="list-style-type: none"> Immune System Disorders: Hypersensitivity reactions (including angioedema, anaphylactic reactions) Eye Disorders: Visual impairment, vision blurred <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm413394.htm</p>
Apixaban <i>Eliquis</i> (Bristol Myers Squibb)	<p>WARNING: Premature discontinuation of <i>Eliquis</i> increases the risk of thrombotic events. Premature discontinuation of any oral anticoagulant, including <i>Eliquis</i>, increases the risk of thrombotic events. If anticoagulation with <i>Eliquis</i> is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.</p> <p>WARNINGS AND PRECAUTIONS</p> <p>Increased Risk of Thrombotic Events after Premature Discontinuation</p> <ul style="list-style-type: none"> Premature discontinuation of any oral anticoagulant, including <i>Eliquis</i>, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from <i>Eliquis</i> to warfarin in clinical trials in atrial fibrillation patients. If <i>Eliquis</i> is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm384790.htm</p>
Axitinib <i>Inlyta</i> (Pfizer)	<p>WARNINGS AND PRECAUTIONS</p> <p>Cardiac Failure</p> <ul style="list-style-type: none"> In a controlled clinical study with <i>Inlyta</i> for the treatment of patients with renal cell carcinoma (RCC), cardiac failure was reported in 6/359 patients (2%) receiving <i>Inlyta</i> and 3/355 patients (1%) receiving sorafenib. Grade 3/4 cardiac failure was observed in 2/359 patients (1%) receiving <i>Inlyta</i> and 1/355 patients (<1%) receiving sorafenib. Fatal cardiac failure was reported in 2/359 patients (1%) receiving <i>Inlyta</i> and 1/355 patients (<1%) receiving sorafenib. Monitor for signs or symptoms of cardiac failure throughout treatment with <i>Inlyta</i>. Management of cardiac failure may require permanent discontinuation of <i>Inlyta</i>. <p>PATIENT COUNSELING INFORMATION</p> <p>Cardiac Failure</p> <ul style="list-style-type: none"> Advise patients that cardiac failure may develop during <i>Inlyta</i> treatment and that signs or symptoms of cardiac failure should be regularly monitored for during treatment. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm372723.htm</p>
Bupropion hydrochloride SR <i>Zyban</i> (GlaxoSmithKline)	<p>Risk of angle-closure glaucoma added to Warning and Precautions, Adverse Reactions, Patient Counseling Information and Medication Guide sections.</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm229405.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
Dapagliflozin <i>Farxiga</i> (AstraZeneca)	<p>DRUG INTERACTIONS</p> <p>Positive Urine Glucose Test</p> <ul style="list-style-type: none"> Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 inhibitors as SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests. Use alternative methods to monitor glycemic control. <p>Interference with 1,5-anhydroglucitol (1,5-AG) Assay</p> <ul style="list-style-type: none"> Monitoring glycemic control with 1,5-AG assay is not recommended as measurements of 1,5AG are unreliable in assessing glycemic control in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm413415.htm</p>
Estradiol vaginal ring <i>Estring</i> (Pharmacia & Upjohn)	<p>BOXED WARNING</p> <ul style="list-style-type: none"> Updated the Boxed Warning to include a revised general heading and 2 specific subheadings: Estrogen-Alone Therapy and Estrogen Plus Progestin Therapy; updated the text in the Boxed Warning to reflect the current recommended estrogen-class labeling. <p>CONTRAINDICATIONS</p> <ul style="list-style-type: none"> Known anaphylactic reaction or angioedema or hypersensitivity to <i>Estring</i> Known protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders <p>WARNINGS</p> <p>Cardiovascular Disorders - Stroke</p> <ul style="list-style-type: none"> Subgroup analyses of women 50 to 59 years of age suggest no increased risk of stroke for those women receiving conjugated estrogen (CE) (0.625 mg) alone versus those receiving placebo (18 vs 21 per 10,000 women-years). <p>Cardiovascular Disorders - Coronary Heart Disease</p> <ul style="list-style-type: none"> Subgroup analyses of women 50 to 59 years of age suggest a statistically nonsignificant reduction in coronary heart disease events (CE [0.625 mg] alone compared to placebo) in women with less than 10 years since menopause (8 vs 16 per 10,000 women-years). <p>Malignant Neoplasms - Breast Cancer</p> <ul style="list-style-type: none"> Updated to reflect the current recommended estrogen-class labeling. <p>Probable Dementia</p> <ul style="list-style-type: none"> Updated to reflect current recommended estrogen-class labeling. <p>Hereditary Angioedema</p> <ul style="list-style-type: none"> Exogenous estrogens may exacerbate symptoms of angioedema in women with hereditary angioedema. <p>PRECAUTIONS</p> <p>Geriatric Use</p> <ul style="list-style-type: none"> Updated to reflect the findings in The Women’s Health Initiative Studies and The Women’s Health Initiative Memory Study; accompanying text was modified to reflect current recommended estrogen-class labeling. Updated Precautions section to reflect current recommended estrogen-class labeling. <p>ADVERSE REACTIONS</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm413413.htm</p>
Etravirine <i>Intelence</i> (Janssen Pharmaceuticals)	<p>DRUG INTERACTIONS</p> <p>Update Table 3 with information regarding coadministration of etravirine with the following drugs:</p> <ul style="list-style-type: none"> dolutegravir, dolutegravir/darunavir/ritonavir, dolutegravir/lopinavir/ritonavir atazanavir/ritonavir boceprevir <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm239762.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
Hydrocodone bitartrate extended- release <i>Zohydro ER</i> (Zogenix)	<p>BOXED WARNING</p> <p>Neonatal Opioid Withdrawal Syndrome</p> <ul style="list-style-type: none"> • Prolonged use of <i>Zohydro ER</i> during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available... • The concomitant use of <i>Zohydro ER</i> with all cytochrome P450 3A4 inhibitors may result in an increase in hydrocodone plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in hydrocodone plasma concentration. Monitor patients receiving <i>Zohydro ER</i> and any CYP3A4 inhibitor or inducer. <p>WARNINGS AND PRECAUTIONS</p> <p>Neonatal Opioid Withdrawal Syndrome</p> <ul style="list-style-type: none"> • Revised <p>Use in Patients with Head Injury and Increased Intracranial Pressure</p> <ul style="list-style-type: none"> • Revised <p>Use in Patients with Convulsive or Seizure Disorders</p> <ul style="list-style-type: none"> • The hydrocodone in <i>Zohydro ER</i> may aggravate convulsions in patients with convulsive disorders and may induce or aggravate seizures in some clinical settings. Monitor patients with a history of seizure disorders for worsened seizure control during <i>Zohydro ER</i> therapy. <p>Avoidance of Withdrawal</p> <ul style="list-style-type: none"> • Avoid the use of mixed agonist/antagonist (ie, pentazocine, nalbuphine, and butorphanol) or partial agonist (buprenorphine) analgesics in patients who have received, or are receiving, a course of therapy with a full opioid agonist analgesic, including <i>Zohydro ER</i>. In these patients, mixed agonist/antagonist and partial agonist analgesics may reduce the analgesic effect and/or may precipitate withdrawal symptoms. <p>Cytochrome P450 CYP3A4 Inhibitors and Inducers</p> <ul style="list-style-type: none"> • Since the CYP3A4 isoenzyme plays a major role in the metabolism of <i>Zohydro ER</i>, drugs that alter CYP3A4 activity may cause changes in clearance of hydrocodone that could lead to changes in hydrocodone plasma concentrations. • Inhibition of CYP3A4 activity by its inhibitors such as macrolide antibiotics (eg, erythromycin), azole-antifungal agents (eg, ketoconazole), and protease inhibitors (eg, ritonavir) may increase plasma concentrations of hydrocodone and prolong opioid effects. • CYP3A4 inducers, such as rifampin, carbamazepine, and phenytoin, may induce the metabolism of hydrocodone and, therefore, may cause increased clearance of the drug that could lead to a decrease in hydrocodone plasma concentrations, lack of efficacy, or, possibly, development of an abstinence syndrome in a patient who had developed physical dependence to hydrocodone. • If co-administration is necessary, monitor patients closely who are currently taking, or discontinuing, CYP3A4 inhibitors or inducers. Evaluate these patients at frequent intervals and consider dose adjustments until stable drug effects are achieved. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm413496.htm</p>
Levetiracetam <i>Keppra XR</i> (UCB)	<p>Pediatric safety data added to the Psychiatric Reactions, Hematologic Abnormalities, and Clinical Trials sections.</p> <p>ADVERSE REACTIONS</p> <p>Postmarketing Experience: Hyponatremia</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm413499.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
Panitumumab <i>Vectibix</i> (Amgen)	<p>WARNINGS AND PRECAUTIONS</p> <p>Dermatologic and Soft Tissue Toxicity</p> <ul style="list-style-type: none"> It could not be determined whether these mucocutaneous adverse reactions were directly related to EGFR inhibition or to idiosyncratic immune-related effects (eg, Stevens Johnson syndrome or toxic epidermal necrolysis). <p>ADVERSE REACTIONS</p> <p>Postmarketing Experience</p> <p>Skin and subcutaneous tissue disorders:</p> <ul style="list-style-type: none"> Life threatening and fatal bullous mucocutaneous disease <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm319207.htm</p>
Paricalcitol <i>Zemiplar</i> (AbbVie)	<p>WARNINGS AND PRECAUTIONS</p> <p>Laboratory Tests</p> <ul style="list-style-type: none"> In pre-dialysis patients, <i>Zemiplar</i> capsules may increase serum creatinine and therefore decrease the estimated GFR. Similar effects have also been seen with calcitriol. <p>ADVERSE REACTIONS</p> <p>Postmarketing Experience: Addition of blood creatinine increase; hypercalcemia</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm413493.htm</p>
Peginterferon alfa-2b <i>Sylatron</i> (Schering)	<p>USE IN SPECIFIC POPULATIONS</p> <p>Renal Impairment</p> <ul style="list-style-type: none"> Reduce the dose of <i>Sylatron</i> by 25% in patients with moderate renal impairment (CLcr 30 to 50 mL/min/1.73m²) and 50% in patients with severe renal impairment (CLcr < 30 mL/min/1.73m²) or end-stage renal disease (ESRD) requiring dialysis. A study in subjects with varying degrees of renal impairment showed that the mean exposure (AUC) to peginterferon alfa-2b increased in subjects with moderate and severe renal impairment or ESRD requiring dialysis, as compared to subjects with normal renal function (CLcr > 80 mL/min/1.73m²) following a single 4.5 mcg/kg dose of peginterferon alfa-2b. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm314604.htm</p>
Ropinirole <i>Requip XL</i> (GlaxoSmithKline)	<p>WARNINGS AND PRECAUTIONS</p> <p>Hallucinations/Psychotic-like Behavior</p> <ul style="list-style-type: none"> Postmarketing reports indicate that patients may experience new or worsening mental status and behavioral changes, which may be severe, including psychotic-like behavior during treatment with ropinirole or after starting or increasing the dose of ropinirole. Other drugs prescribed to improve the symptoms of Parkinson’s disease can have similar effects on thinking and behavior. This abnormal thinking and behavior can consist of one or more of a variety of manifestations including paranoid ideation, delusions, hallucinations, confusion, psychotic-like behavior, disorientation, aggressive behavior, agitation, and delirium. Patients with a major psychotic disorder should ordinarily not be treated with <i>Requip XL</i> because of the risk of exacerbating the psychosis. In addition, certain medications used to treat psychosis may exacerbate the symptoms of Parkinson’s disease and may decrease the effectiveness of <i>Requip XL</i>. <p>Impulse Control/Compulsive Behaviors</p> <ul style="list-style-type: none"> Case reports suggest that patients can experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge or compulsive eating, and/or other intense urges, and the inability to control these urges while taking one or more of the medications, including <i>Requip XL</i>, that increase central dopaminergic tone and that are generally used for the treatment of Parkinson’s disease. In some cases, although not all, these urges were reported to have stopped when the dose was reduced or the medication

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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>was discontinued. Because patients may not recognize these behaviors as abnormal, it is important for prescribers to specifically ask patients or their caregivers about the development of new or increased gambling urges, sexual urges, uncontrolled spending, binge or compulsive eating, or other urges while being treated with <i>Requip XL</i>. Physicians should consider dose reduction or stopping the medication if a patient develops such urges while taking <i>Requip XL</i>.</p> <p>ADVERSE REACTIONS Addition or modification of information related to hypersensitivity; somnolence; psychotic-like behavior; impulse control/compulsive behaviors; withdrawal-emergent hyperpyrexia and confusion; melanoma; and fibrotic complications http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm413475.htm</p>
Somatropin [rDNA origin] <i>Omnitrope</i> (Sandoz)	<p>WARNINGS AND PRECAUTIONS Neoplasms</p> <ul style="list-style-type: none"> Revisions regarding an increased risk of developing a second neoplasm in childhood cancer survivors treated with radiation to the brain/head for their first neoplasm and who developed subsequent growth hormone deficiency and were treated with somatropin <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm255097.htm</p>
Taliglucerase alfa <i>Elelyso</i> (Pfizer)	<p>WARNINGS AND PRECAUTIONS Hypersensitivity Reactions Including Anaphylaxis</p> <ul style="list-style-type: none"> Serious hypersensitivity reactions, including anaphylaxis, have occurred in some patients treated with <i>Elelyso</i>. In clinical trials, 2 of 72 (2.8%) patients treated with <i>Elelyso</i> experienced signs and symptoms consistent with anaphylaxis. Signs and symptoms of these patients included urticaria, hypotension, flushing, wheezing, chest tightness, nausea, vomiting, and dizziness. These reactions occurred during <i>Elelyso</i> infusion. In clinical trials with <i>Elelyso</i>, 21 of 72 (29%) patients experienced hypersensitivity reactions, including anaphylaxis. Signs and symptoms of hypersensitivity reactions included pruritus, angioedema, flushing, erythema, rash, nausea, vomiting, cough, chest tightness, and throat irritation. These reactions have occurred up to 3 hours after the start of infusion. Due to the potential for anaphylaxis, appropriate medical support should be readily available when <i>Elelyso</i> is administered. Observe patients closely for an appropriate period of time after administration of <i>Elelyso</i>, taking into account the time to onset of anaphylaxis seen in clinical trials. Inform patients of the signs and symptoms of anaphylaxis, and instruct them to seek immediate medical care should signs and symptoms occur. If anaphylaxis occurs, <i>Elelyso</i> should be immediately discontinued, and appropriate medical treatment should be initiated. Management of hypersensitivity reactions should be based on the severity of the reaction and include slowing or temporary interruption of the infusion and/or administration of antihistamines, antipyretics, and/or corticosteroids for mild reactions. Pretreatment with antihistamines and/or corticosteroids may prevent subsequent hypersensitivity reactions. Patients were not routinely premedicated prior to infusion of <i>Elelyso</i> during clinical studies. If severe hypersensitivity reactions occur, immediately stop the infusion of <i>Elelyso</i> and initiate appropriate treatment. Consider the risks and benefits of re-administering <i>Elelyso</i> in patients who have experienced a severe reaction associated with <i>Elelyso</i>. Caution should be exercised upon rechallenge, and appropriate medical support should be readily available. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm413395.htm</p>

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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
Valproic acid <i>Stavzor</i> (Banner Pharmacaps)	<p>ADVERSE REACTIONS</p> <p>Postmarketing Experience</p> <ul style="list-style-type: none"> • Musculoskeletal: Fractures, decreased bone mineral density, osteopenia, osteoporosis <p>USE IN SPECIFIC POPULATIONS</p> <p>Pregnancy: Fetal Risk Summary</p> <ul style="list-style-type: none"> • An observational study has suggested that exposure to valproate products during pregnancy may increase the risk of autism spectrum disorders. In this study, children born to mothers who had used valproate products during pregnancy had 2.9 times the risk (95% confidence interval [CI], 1.7-4.9) of developing autism spectrum disorders compared to children born to mothers not exposed to valproate products during pregnancy. The absolute risks for autism spectrum disorders were 4.4% (95% CI, 2.6%-7.5%) in valproate-exposed children and 1.5% (95% CI, 1.5%-1.6%) in children not exposed to valproate products. Because the study was observational in nature, conclusions regarding a causal association between in utero valproate exposure and an increased risk of autism spectrum disorder cannot be considered definitive. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm360495.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. ■