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): September 16, 2014 through October 15, 2014

Cobicistat – Tybost (Gilead)	
<i>Comparative agents:</i>	Original part of a 4-drug combination product (<i>Stribild</i>)
<i>Indication:</i>	Increase systemic exposure of atazanavir or darunavir (once-daily dosing regimen) in combination with other antiretroviral agents in the treatment of HIV-1 infection. Coadministered with atazanavir or darunavir at the same time, with food, and in combination with other HIV-1 antiretroviral agents.
<i>Mechanism of action:</i>	CYP3A inhibitor
<i>Common adverse effects:</i>	Jaundice, ocular icterus, nausea
<i>Dosage form & strength:</i>	Tablets; 150 mg
<i>Product labeling:</i>	www.accessdata.fda.gov/drugsatfda_docs/label/2014/203094s000lbl.pdf
Dulaglutide – Trulicity (Lilly)	
<i>Comparative agents:</i>	Albiglutide, exenatide, liraglutide
<i>Indication:</i>	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
<i>Mechanism of action:</i>	GLP-1 receptor agonist
<i>Common adverse effects:</i>	Nausea, diarrhea, vomiting, abdominal pain, and decreased appetite
<i>Dosage form & strength:</i>	Injectable; 0.75 mg/mL & 1.5 mg/mL
<i>Product labeling:</i>	http://pi.lilly.com/us/trulicity-uspi.pdf

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

Elvitegravir – Vitekta (Gilead)	
<i>Comparative agents:</i>	Original part of a 4-drug combination product (<i>Stribild</i>)
<i>Indication:</i>	Treatment of HIV-1 infection in antiretroviral treatment-experienced adults. Must be used in combination with an HIV protease inhibitor coadministered with ritonavir and another antiretroviral drug.
<i>Mechanism of action:</i>	HIV-1 integrase strand transfer inhibitor
<i>Common adverse effects:</i>	Diarrhea
<i>Dosage form & strength:</i>	Tablets; 85 mg and 150 mg
<i>Product labeling:</i>	www.accessdata.fda.gov/drugsatfda_docs/label/2014/203093s000lbl.pdf
Immune globulin infusion (human)/recombinant human hyaluronidase – HyQvia (Baxter Healthcare Corporation)	
<i>Comparative agents:</i>	Individual ingredients
<i>Indication:</i>	Treatment of primary immunodeficiency (PI) in adults
<i>Mechanism of action:</i>	Immune globulin with a recombinant human hyaluronidase
<i>Common adverse effects:</i>	Local reactions, headache, antibody formation against recombinant human hyaluronidase (rHuPH20), fatigue, nausea, pyrexia, and vomiting
<i>Dosage form & strength:</i>	Vial; 10% IgG (100 mg/mL/recombinant human hyaluronidase 160 U/mL)
<i>Product labeling:</i>	http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/UCM414440.pdf
Ledipasvir/sofosbuvir – Harvoni (Gilead Sciences, Inc)	
<i>Comparative agents:</i>	Sofosbuvir/peginterferon alfa-2a/ribavirin
<i>Indication:</i>	Treatment of chronic hepatitis C genotype 1 infection in adults
<i>Mechanism of action:</i>	NS5A inhibitor plus a hepatitis C virus nucleotide analog NS5B polymerase inhibitor
<i>Common adverse effects:</i>	Fatigue and headache
<i>Dosage form & strength:</i>	Tablets; ledipasvir 90 mg / sofosbuvir 400 mg
<i>Product labeling:</i>	http://www.gilead.com/~media/Files/pdfs/medicines/liver-disease/harvoni/harvoni_pi.pdf
Naloxegol – Movantik (AstraZeneca/Nektar Therapeutics)	
<i>Comparative agents:</i>	Methylnaltrexone; naltrexone
<i>Indication:</i>	Treatment of opioid-induced constipation in adult patients with chronic, noncancer pain
<i>Mechanism of action:</i>	Peripherally acting mu-opioid receptor antagonist
<i>Common adverse effects:</i>	Abdominal pain, diarrhea, nausea, flatulence, vomiting, headache, hyperhidrosis, and back pain
<i>Dosage form & strength:</i>	Tablet; 12.5 & 25 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/204760s000lbl.pdf

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

Netupitant/palonosetron – Akynzeo (Eisai)	
<i>Comparative agents:</i>	Individual ingredients
<i>Indication:</i>	Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy
<i>Mechanism of action:</i>	Palonosetron prevents nausea and vomiting during the acute phase and netupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.
<i>Common adverse effects:</i>	Headache, asthenia, dyspepsia, fatigue, constipation, and erythema
<i>Dosage form & strength:</i>	Capsule; netupitant 300 mg / palonosetron 0.5 mg
<i>Product labeling:</i>	http://www.akynzeo.com/media/Prescribing_Information.pdf
Nintedanib – Ofev (Boehringer Ingelheim)	
<i>Comparative agents:</i>	None
<i>Indication:</i>	Treatment of idiopathic pulmonary fibrosis
<i>Mechanism of action:</i>	Kinase inhibitor
<i>Common adverse effects:</i>	Diarrhea, nausea, abdominal pain, vomiting, liver enzyme elevation, decreased appetite, headache, decreased weight, and high blood pressure
<i>Dosage form & strength:</i>	Capsule; 100 & 150 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205832s000lbl.pdf
Pirfenidone – Esbriet (Genentech)	
<i>Comparative agents:</i>	None
<i>Indication:</i>	Treatment of idiopathic pulmonary fibrosis
<i>Mechanism of action:</i>	Anti-fibrotic and anti-inflammatory properties
<i>Common adverse effects:</i>	Nausea, rash, abdominal pain, upper respiratory tract infection, diarrhea, fatigue, headache, dyspepsias, dizziness, vomiting, decreased/loss of appetite, gastroesophageal reflux disease, sinusitis, insomnia, decreased weight, and arthralgia.
<i>Dosage form & strength:</i>	Capsule; 267 mg
<i>Product labeling:</i>	http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/022535s000lbl.pdf

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

Generic name	Brand name (Company)	Indication and comments
New dosage forms/strength/ route of administration		
Tiotropium bromide	<i>Spiriva Respimat</i> (Boehringer Ingelheim)	Mist formulation using the <i>Respimat</i> delivery system that is indicated for long-term, once-daily maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease
New indications		
Adalimumab	<i>Humira</i> (AbbVie)	Treat pediatric patients age 6 years and older afflicted with moderately to severely active Crohn's disease who have not responded adequately to prior treatment with corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine, or methotrexate
Avanafil	<i>Stendra</i> (VIVUS)	Labeling changed that the drug can be taken approximately 15 minutes before sexual activity, instead of about 30 minutes
Budesonide	<i>Uceris</i> (Salix Pharmaceuticals)	Induction of remission in patients afflicted with active mild-to-moderate distal ulcerative colitis extending up to 40 cm from the anal verge
Methylnaltrexone bromide	<i>Relistor</i> (Salix Pharmaceuticals)	Treatment of opioid-induced constipation in patients receiving opioids for chronic noncancer pain
Otezla	<i>Apremilast</i> (Celgene)	Treatment of patients with moderate to severe plaque psoriasis for who phototherapy or systemic therapy is appropriate

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

Generic name	Brand name (Company)	Indication and comments
Recommended for approval by an FDA advisory panel		
Recombinant human parathyroid hormone (rhPTH [1-84])	<i>Natpara</i> (NPS Pharmaceuticals)	Positive advisory panel vote of 8 to 5; PDUFA scheduled for October 24, 2014
Recommended for NON-approval by an FDA advisory panel		
Testosterone	<i>Textoro</i> (Clarus Therapeutics)	Negative advisory panel vote of 12 to 8; PDUFA scheduled for November 3, 2014

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

Generic name <i>Brand name</i> (Company)	Warning
Alglucosidase alfa <i>Lumizyme</i> (Genzyme)	Extensive changes in the Boxed Warning, Warnings and Precaution, and Adverse Reaction sections. Pregnancy category changed from B to C. Nursing mothers: Case reported for enzymatic activity in child. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm314609.htm
Bimatoprost <i>Latisse</i> (Allergan)	WARNINGS AND PRECAUTIONS Use with Contact Lenses: Product contains benzalkonium chloride, which may be absorbed by and cause discoloration of soft contact lenses. ADVERSE REACTIONS Clinical Studies Experience: The most frequently reported adverse reactions were eye pruritus, conjunctival hyperemia, skin hyperpigmentation, ocular irritation, dry eye symptoms, and periorbital erythema. These reactions occurred in less than 4% of patients. Postmarketing Experience: Possible causal connection to <i>Latisse</i> or a combination of factors include: eye swelling, eyelid edema, hypersensitivity (local allergic reactions), lacrimation increased, and madarosis. USE IN SPECIFIC POPULATIONS: Pediatric Use <ul style="list-style-type: none"> Use of <i>Latisse</i> was evaluated in a 16-week double-masked, randomized, vehicle-controlled study conducted in pediatric patients who were post chemotherapy or had alopecia areata, and adolescents who had hypotrichosis with no associated medical condition. No new safety issues were observed. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm275785.htm
Bimatoprost ophthalmic solution <i>Lumigan</i> (Allergan)	WARNINGS AND PRECAUTIONS: Intraocular Inflammation <ul style="list-style-type: none"> Prostaglandin analogs, including bimatoprost, have been reported to cause intraocular inflammation. In addition, because these products may exacerbate inflammation, caution should be use in patients with active intraocular inflammation (eg, uveitis). http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm418727.htm
Dexamethasone intravitreal implant <i>Ozurdex</i> 0.7 mg (Allergan)	CONTRAINDICATIONS Glaucoma: <i>Ozurdex</i> is contraindicated in patients with glaucoma, who have cup to disc ratios of greater than 0.8. Torn or Ruptured Posterior Lens Capsule: <i>Ozurdex</i> is contraindicated in patients whose posterior lens capsule is torn or ruptured because of the risk of migration into the anterior chamber. Laser posterior capsulotomy in pseudophakic patients is not a contraindication for <i>Ozurdex</i> use. Hypersensitivity: <i>Ozurdex</i> is contraindicated in patients with known hypersensitivity to any components of this product. WARNINGS AND PRECAUTIONS Steroid-related Effects: Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection. ADVERSE REACTIONS Clinical Studies Experience: Revised to include revised intraocular pressure data and adverse reaction data for the diabetic macular edema indication. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm295117.htm

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

Diclofenac sodium/misoprostol <i>Arthrotec</i> (Pfizer)	<p>CONTRAINDICATIONS</p> <ul style="list-style-type: none"> • Add contraindication for patients with active gastrointestinal bleeding. <p>WARNINGS</p> <ul style="list-style-type: none"> • Add that the use of diclofenac/misoprostol with concomitant nonsteroidal anti-inflammatory drugs (NSAIDs) including COX-2 inhibitors should be avoided. • Skin Reactions subsection was expanded. <p>PRECAUTIONS</p> <ul style="list-style-type: none"> • Remove statement that nursing mothers, since these patients should not take <i>Arthrotec</i>. <p>Drug Interactions</p> <ul style="list-style-type: none"> • Revise statement about renal function in ACE inhibitors subsection. • Add Tacrolimus subsection. <p>ADVERSE REACTIONS:</p> <ul style="list-style-type: none"> • Add the following subsections: Pregnancy, puerperium and perinatal conditions; Congenital, familial and genetic disorders. • Expand upon the following subsections: Body as whole; female reproductive disorders; hemic and lymphatic system; metabolic and nutritional; skin and appendages; and urinary. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm239819.htm</p>
Docetaxel injection concentrate (Actavis)	<p>WARNINGS AND PRECAUTIONS</p> <p>Eye Disorders</p> <ul style="list-style-type: none"> • Cystoid macular edema (CME) has been reported in patients treated with docetaxel injection concentrate. Patients with impaired vision should undergo a prompt and comprehensive ophthalmologic examination. If CME is diagnosed, docetaxel injection concentrate treatment should be discontinued and appropriate treatment initiated. Alternative non-taxane cancer treatment should be considered. <p>Alcohol Content</p> <ul style="list-style-type: none"> • Cases of intoxication have been reported with some formulations of docetaxel due to the alcohol content. The alcohol content in a dose of docetaxel injection concentrate may affect the central nervous system and should be taken into account for patients in whom alcohol intake should be avoided or minimized. Consideration should be given to the alcohol content in docetaxel injection, concentrating on the ability to drive or use machines immediately after the infusion. • Each administration of docetaxel injection concentrate at 100 mg/m² delivers 4.75 g/m² of ethanol. For a patient with a body surface area (BSA) of 2.0 m², this would deliver 9.5 grams of ethanol. Other docetaxel products may have a different amount of alcohol. <p>ADVERSE REACTIONS: Postmarketing Experience</p> <ul style="list-style-type: none"> • Ophthalmologic: Cases of CME have been reported in patients treated with docetaxel injection concentrate. • Respiratory: Dyspnea, acute pulmonary edema, acute respiratory distress syndrome/pneumonitis, interstitial lung disease, interstitial pneumonia, respiratory failure, and pulmonary fibrosis have rarely been reported and may be associated with fatal outcome. Rare cases of radiation pneumonitis have been reported in patients receiving concomitant radiotherapy. • Metabolism and nutrition disorders: Cases of hyponatremia have been reported. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm418721.htm</p>

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

<p>Lenalidomide <i>Revlimid</i> (Celgene Corporation)</p>	<p>BOXED WARNING: Venous and Arterial Thromboembolism</p> <ul style="list-style-type: none"> Increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE), as well as risk of myocardial infarction and stroke in patients with multiple myeloma receiving <i>Revlimid</i> with dexamethasone. <p>WARNINGS AND PRECAUTIONS: Venous and Arterial Thromboembolism</p> <ul style="list-style-type: none"> Venous thromboembolic events (DVT and PE) and arterial thromboses are increased in patients treated with <i>Revlimid</i>. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm299519.htm</p>
<p>Lidocaine HCl <i>Xylocaine</i> viscous solution (Fresenius Kabi)</p>	<p>BOXED WARNING: Life-threatening and fatal events in infants and young children</p> <ul style="list-style-type: none"> Postmarketing cases of seizures, cardiopulmonary arrest, and death in patients under the age of 3 years have been reported with use of <i>Xylocaine</i> 2% viscous solution when it was not administered in strict adherence to the dosing and administration recommendations. In the setting of teething pain, <i>Xylocaine</i> 2% viscous solution should generally not be used. For other conditions, the use of the product in patients less than 3 years of age should be limited to those situations where safer alternatives are not available or have been tried but failed. To decrease the risk of serious adverse events with use of <i>Xylocaine</i> 2%, instruct caregivers to strictly adhere to the prescribed dose and frequency of administration and store the prescription bottle safely out of reach of children. <p>WARNINGS: Life-threatening and fatal events in infants and young children</p> <ul style="list-style-type: none"> Postmarketing cases of seizures, cardiopulmonary arrest, and death in patients under the age of 3 years <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm417582.htm</p>
<p>Losartan potassium/ hydrochlorothiazide <i>Hyzaar</i> (Merck)</p>	<p>WARNINGS Lithium Toxicity: Monitor serum lithium levels in patients receiving lithium and hydrochlorothiazide.</p> <p>PRECAUTIONS Drug Interactions, Losartan Potassium – Lithium: Increases in serum lithium concentrations and lithium toxicity have been reported during concomitant administration of lithium with angiotensin II receptor antagonists. Monitor serum lithium levels during concomitant use.</p> <p>Dual Blockade of the Renin-Angiotensin System (RAS)</p> <ul style="list-style-type: none"> Patients receiving the combination of losartan and lisinopril did not obtain any additional benefit compared to monotherapy for the combined endpoint of decline in glomerular filtration rate (GFR), end-stage renal disease, or death, but experienced an increased incidence of hyperkalemia and acute kidney injury compared with the monotherapy group. Closely monitor blood pressure, renal function, and electrolytes in patients on <i>Hyzaar</i> and other agents that affect the RAS. <p>Drug Interactions, Hydrochlorothiazide – Lithium: Should not generally be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Monitor serum lithium levels during concomitant use. Refer to the package insert for lithium preparations before use of such preparations with <i>Hyzaar</i>.</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm169677.htm</p>
<p>Peginterferon alfa-2a <i>Pegasys</i> (Genentech)</p>	<p>Ribavirin information removed from Boxed Warning.</p> <p>New contraindications: All contraindications of other drugs used in the treatment of hepatitis C apply to combination therapy with peginterferon alfa-2a; ribavirin is contraindicated in pregnant women and men whose female partners are pregnant.</p> <p>Warnings and Precautions: Warnings and precautions related to the other drugs used in the treatment of hepatitis C apply to combination therapy with peginterferon alfa-2a.</p> <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm247047.htm</p>

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

Regadenoson <i>Lexiscan</i> injection for intravenous use (Astellas Pharma)	<p>WARNINGS AND PRECAUTIONS</p> <p>Atrial Fibrillation/Atrial Flutter</p> <ul style="list-style-type: none"> New-onset or recurrent atrial fibrillation with rapid ventricular response and atrial flutter have been reported following <i>Lexiscan</i> injection. <p>Seizure</p> <ul style="list-style-type: none"> <i>Lexiscan</i> may lower the seizure threshold. New-onset or recurrence of convulsive seizures has occurred following <i>Lexiscan</i> injection. Some seizures are prolonged and require emergent anticonvulsive management. Aminophylline may increase the risk of seizures associated with <i>Lexiscan</i> injection. Methylxanthine use is not recommended in patients who experience a seizure in association with <i>Lexiscan</i> administration. <p>Cerebrovascular Accident (Stroke)</p> <ul style="list-style-type: none"> Hemorrhagic and ischemic cerebrovascular accidents have occurred. Hemodynamic effects of <i>Lexiscan</i> including hypotension or hypertension may be associated with these adverse reactions. <p>Postmarketing Experience:</p> <p>Cardiovascular</p> <ul style="list-style-type: none"> Myocardial infarction, cardiac arrest, ventricular arrhythmias, supraventricular tachyarrhythmias including atrial fibrillation with rapid ventricular response (new-onset or recurrent), atrial flutter, heart block (including third-degree block), asystole, marked hypertension, symptomatic hypotension in association with transient ischemic attack, seizures, and syncope. <p>Central Nervous System</p> <ul style="list-style-type: none"> Tremor, seizure, transient ischemic attack, and cerebrovascular accident including intracranial hemorrhage <p>DRUG INTERACTIONS: Methylxanthines (eg, caffeine, aminophylline, and theophylline) are nonspecific adenosine receptor antagonists that interfere with the vasodilation activity of <i>Lexiscan</i>. Patients should avoid consumption of any products containing methylxanthines as well as any drugs containing theophylline or aminophylline for at least 12 hours before <i>Lexiscan</i> administration. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm418726.htm</p>
Serotonin-3 (5-HT ₃) receptor antagonists: dolasetron, granisetron, ondansetron, palonosetron	<p>Change in the Class: WARNINGS AND PRECAUTIONS</p> <p>Serotonin Syndrome</p> <ul style="list-style-type: none"> The development of serotonin syndrome has been reported with 5-HT₃ receptor antagonists. Most reports have been associated with concomitant use of serotonergic drugs (eg, selective serotonin reuptake inhibitors [SSRIs], serotonin and norepinephrine reuptake inhibitors [SNRIs], monoamine oxidase inhibitors, mirtazapine, fentanyl, lithium, tramadol, and intravenous methylene blue). Some of the reported cases were fatal. Serotonin syndrome occurring with overdose of another 5-HT₃ receptor antagonist alone has also been reported. The majority of reports of serotonin syndrome related to 5-HT₃ receptor antagonist use occurred in a postanesthesia care unit or an infusion center. Symptoms associated with serotonin syndrome may include the following combination of signs and symptoms: mental status changes (eg, agitation, hallucinations, delirium, and coma), autonomic instability (eg, tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, and hyperthermia), neuromuscular symptoms (eg, tremor, rigidity, myoclonus, hyperreflexia, and incoordination), and seizures, with or without gastrointestinal symptoms (eg, nausea, vomiting, and diarrhea). Patients should be monitored for the emergence of serotonin syndrome, especially with concomitant use of <drug name> and other serotonergic drugs. If symptoms of serotonin syndrome occur, discontinue <drug name> and initiate supportive treatment. Patients should be informed of the increased risk of serotonin syndrome, especially if <drug name> is used concomitantly with other serotonergic drugs. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm418818.htm</p>

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

Somatropin [rDNA origin] <i>Genotropin</i> for injection (Pfizer)	<p>WARNINGS AND PRECAUTIONS: Neoplasms</p> <ul style="list-style-type: none"> • In childhood cancer survivors who were treated with radiation to the brain/head for their first neoplasm and who developed subsequent growth hormone deficiency (GHD) and were treated with somatropin, an increased risk of a second neoplasm has been reported. Intracranial tumors, in particular meningiomas, were the most common of these second neoplasms. In adults, it is unknown whether there is any relationship between somatropin replacement therapy and CNS tumor recurrence. • Monitor all patients with a history of GHD secondary to an intracranial neoplasm routinely while on somatropin therapy for progression or recurrence of the tumor. Because children with certain rare genetic causes of short stature have an increased risk of developing malignancies, practitioners should thoroughly consider the risks and benefits of starting somatropin in these patients. If treatment with somatropin is initiated, these patients should be carefully monitored for development of neoplasms. Monitor patients on somatropin therapy carefully for increased growth, or potential malignant changes, of preexisting nevi. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm203732.htm</p>
Somatropin [rDNA origin] <i>Norditropin</i> injection (Novo Nordisk)	<p>WARNINGS AND PRECAUTIONS: Neoplasms</p> <ul style="list-style-type: none"> • In childhood cancer survivors who were treated with radiation to the brain/head for their first neoplasm and who developed subsequent GHD and were treated with somatropin, an increased risk of a second neoplasm has been reported. Intracranial tumors, in particular meningiomas, were the most common of these second neoplasms. In adults, it is unknown whether there is any relationship between somatropin replacement therapy and CNS tumor recurrence. • Monitor all patients with a history of GHD secondary to an intracranial neoplasm routinely while on somatropin therapy for progression or recurrence of the tumor. Because children with certain rare genetic causes of short stature have an increased risk of developing malignancies, practitioners should thoroughly consider the risks and benefits of starting somatropin in these patients. If treatment with somatropin is initiated, these patients should be carefully monitored for development of neoplasms. Monitor patients on somatropin therapy carefully for increased growth, or potential malignant changes, of preexisting nevi. <p>http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm258783.htm</p>
Triazolam <i>Halcion</i> (Pfizer)	<p>CONTRAINDICATIONS</p> <ul style="list-style-type: none"> • Use with medications that significantly impair the oxidative metabolism mediated by cytochrome P450 3A (CYP 3A) including ketoconazole, itraconazole, nefazodone, and several HIV protease inhibitors. <p>WARNINGS</p> <ul style="list-style-type: none"> • Potent CYP 3A inhibitors: Potent inhibitors of CYP 3A that should not be used concomitantly with triazolam include ketoconazole, itraconazole, and nefazodone and several HIV protease inhibitors (eg, ritonavir) including indinavir, nelfinavir, and saquinavir. Although data concerning the effects of azole-type antifungal agents other than ketoconazole and itraconazole on triazolam metabolism are not available, they should be considered potent CYP 3A inhibitors, and their coadministration with triazolam is not recommended. <p>PRECAUTIONS</p> <ul style="list-style-type: none"> • Drugs that inhibit triazolam metabolism via cytochrome P450 3A: The initial step in triazolam metabolism is hydroxylation catalyzed by cytochrome P450 3A (CYP 3A). Drugs that inhibit this metabolic pathway may have a profound effect on the clearance of triazolam (see CONTRAINDICATIONS and WARNINGS for additional drugs of this type). <i>Halcion</i> is contraindicated with ketoconazole, itraconazole, nefazodone, and several HIV protease inhibitors.

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

	<p>MEDICATION GUIDE</p> <ul style="list-style-type: none"> Added <i>Halcion</i> should not be taken with some drugs including ketoconazole, itraconazole, nefazodone, ritonavir, indinavir, nelfinavir, saquinavir, or lopinavir. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm418718.htm
Varenicline <i>Chantix</i> (Pfizer)	<p>WARNINGS AND PRECAUTIONS</p> <p>Neuropsychiatric Symptoms and Suicidality: Extensive changes</p> <p>Seizures</p> <ul style="list-style-type: none"> During clinical trials and the postmarketing experience, there have been reports of seizures in patients treated with <i>Chantix</i>. Some patients had no history of seizures, whereas others had a history of seizure disorder that was remote or well-controlled. In most cases, the seizure occurred within the first month of therapy. <p>Interaction with Alcohol</p> <ul style="list-style-type: none"> Postmarketing reports of patients experiencing increased intoxicating effects of alcohol while taking <i>Chantix</i>. Some cases described unusual and sometimes aggressive behavior, and were often accompanied by amnesia for the events. Advise patients to reduce the amount of alcohol they consume while taking <i>Chantix</i> until they know whether <i>Chantix</i> affects their tolerance for alcohol. http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm240390.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.