Highlights of FDA Activities – 9/1/14 – 9/30/14

FDA Drug Safety Communications & Drug Information Updates:

Medical Device Safety and Recalls: Customed Inc., Surgical Convenience Packs - Damaged Packaging [09/05/14]
Customed Inc., Surgical Convenience Packs have been recalled as a result of potentially compromised sterility due to individual packs adhering to one another inside the shipping case. In some cases, the plastic packaging of one bag (along the printed words "SNAP SMARTLY TO OPEN") has adhered to the end seal of an adjacent pack. When the bags are separated, the plastic film can tear and compromise the sterility of the contents. There is significant risk of compromised sterility and use of a contaminated product, whether the package is damaged or not. In addition, the products have been exposed to uncontrolled and inadequate storage conditions and serious deficiencies in the manufacturing process have been noted.

Drug Information Update - FDA Publishes Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations [09/9/14]
The FDA published the Purple Book, a version of the Orange Book specific to biological products. The book lists biological products licensed by the FDA, including any biosimilar or interchangeable biological product.

Drug Information Update - FDA reminds health care professionals and consumers not to use sterile products from Downing Labs/NuVision Pharmacy of Texas [09/10/14]
The FDA reminded health care professionals and consumers about safety concerns with all sterile-use drug products made and distributed by Downing Labs LLC, doing business as NuVision Pharmacy, in Dallas, Texas. Health care professionals should not use any NuVision/Downing Labs sterile products for their patients because the firm cannot ensure the safety or quality of these products. The FDA has issued a formal request to Downing Labs for the immediate recall of all lots of its purportedly sterile products currently on the market that are not expired. In the letter, the FDA outlined poor conditions and practices identified by FDA investigators during a July 2014 inspection of Downing Labs' Dallas facility.

Drug Information Update – FDA Urges You to Know Your Source for Prescription Drugs [09/23/14]
FDA launched an educational campaign advising health care professionals to only purchase prescription drugs from wholesale drug distributors licensed in their state, watch for offers that are too good to be true (which may indicate the products are stolen, counterfeit, substandard, or unapproved), and ensure received products are FDA-approved. The FDA encourages healthcare professionals to visit FDA's Know Your Source web site.

Xolair (omalizumab): Drug Safety Communication – Slightly Elevated Risk of Cardiovascular and Cerebrovascular Serious Adverse Events [09/26/14]
An FDA review of safety studies with omalizumab noted a slight potential increase in risk of cardiovascular and cerebrovascular events, including transient ischemic attacks, myocardial infarction, unstable angina, pulmonary hypertension, and venous thromboembolism. Labeling will be updated to reflect the possible association. Patients should be advised to continue taking the medication and discuss any concerns with their health care provider.

Major Product Recalls Announced Through MedWatch:

Dermatend Original and Dermatend Ultra: Recall - Safety [09/02/14]
Solace International, Inc. is voluntarily recalling all lots of Dermatend Original and Dermatend Ultra, in all sizes and dosage forms, to the distributor/wholesaler level. These products have been used to remove moles, warts, and skin tags. A mole should be removed under the supervision of a dermatologist. Dermatend is not FDA approved, thus has not been shown to be safe and effective for the uses suggested in the labeling. Using these Dermatend products instead of seeking medical attention could result in delayed diagnosis of conditions such as cancer.

Martin Avenue Pharmacy, Inc. Compounded Sterile Preparations: Recall – Lack of Assurance of Sterility [09/02/14]

Martin Avenue Pharmacy, Inc. is conducting a voluntary recall of all in-date compounded sterile preparations. The recall is being initiated in connection with a recent FDA inspection due to observations associated with certain quality control procedures that present a risk to sterility assurance. Compounded products were distributed to medical professionals and directly to patients in Illinois, Wisconsin, Ohio, Michigan, Florida, Alabama, and Texas.

CloverSnare 4-Loop Vascular Retrieval Snare by Cook Medical (Model #VRS-6.0-9.0) [09/05/14]

A recall has been issued for the Cook CloverSnare 4-Loop Vascular Retrieval Snare due to a potential for the snare loop to separate from the shaft. If this occurs, the snare loop may travel through the vascular system and block blood vessels or become stuck in other organs, such as the heart and lungs. Additional intervention may be necessary to retrieve the separated snare loop from the patient. This failure will also cause the device to stop working. Four injuries have been reported. The use of the affected product may cause serious adverse health consequences, including death.

Pharmacy Creations: Recall – Potential Non-Sterility [09/06/14]

Pharmacy Creations has voluntarily recalled four product lots following receipt of testing results that indicated that the product lots may not be sterile. The prescription preparations were distributed in Florida, New Jersey, New York, and Puerto Rico between March 4, 2014 and June 18, 2014 and were mailed directly to patients and physicians. Products involved were ascorbic acid 500 mg/mL lot #05082014@7, glutathione 100 mg/mL lot #05122014@4, magnesium chloride 200 mg/mL lot #05202014@7, and Tropi/Cyclo/Phenyl/Tobra/Flurb (1/1/10/0.3/0.3)% lot # 05202014@3.

Heparin Sodium 1,000 USP Heparin Units/500 mL (Hospira): Recall – Particulate Matter [09/12/14]

One lot of Heparin Sodium, 1,000 USP Heparin Units/500 mL (2 USP Heparin Units/mL), in 0.9% Sodium Chloride Injection, 500 mL by Hospira recalled (NDC 0409-7620-03; Lot 41-046-JT; expiration date of 01 NOV 2015) due to one confirmed customer report of particulate in a single unit.

Potassium Chloride Injection (Baxter International Inc.): Recall – Shipping Carton Mislabeled [09/17/14]

Potassium Chloride Injection 10 mEq per 100 mL product code 2B0826 (Lot #P318220, NDC #0338-709-48) recalled due to a labeling error on the shipping cartons in a single lot. Shipping cartons labeled for this specific lot number of Potassium Chloride Injection may contain units of Gentamicin Sulfate Injection, 80 mg in 100 mL, product code 2B0862. It is recommended that healthcare professionals carefully review the product label before administering.

Dietary Supplement Recalls & Public Notifications

In September, the FDA issued notifications to the public regarding undeclared active ingredients in the following products. Patients are advised not to purchase or use these products.

Product	***Promoted Use***	***Hidden/Undeclared Drug Ingredient(s)***
RegeneSlim Appetite Control Capsules*	Weight loss	DMAA (AKA 1,3-dimethylamylamine, methylhexanamine, "geranium extract")
Lx1	Weight loss	DMAA
Mezo	Weight loss	Benzylsibutramine (structurally related to sibutramine)
Best Line Suplemento Alimenticio Capsules	Weight loss	Sibutramine
Japan Hokkaido Slimming Weight Loss Pills	Weight loss	Sibutramine, benzocaine, phenolphthalein, and diclofenac
Bo Ying Compound	Influenza, fever, sneezing, nasal discharge	Lead poisoning has been reported in association with this product

*Recalled

New Product Shortages Reported by the FDA:	***Date Initially Posted***
Methylphenidate HCl ER Capsules/Tablets	9/23/14
Sterile Water for Injection Solutions	9/16/14

New Drug Approvals:	***Description***	***Date Approved***
Pembrolizumab / Keytruda / Merck & Co.	See attached drug summary	[9/04/14]
Ferric citrate / Keryx Biopharmaceuticals	See attached drug summary	[9/05/14]
Naltrexone HCl – Bupropion HCl ER/ Contrave / Takeda	See attached drug summary	[9/10/14]
Naloxegol / Movantik / AstraZeneca	See attached drug summary	[9/16/14]
Dulaglutide / Trulicity / Eli Lilly & Co.	See attached drug summary	[9/18/14]

New Indications:	***Description***	***Date Approved***
Meningococcal (groups A, C, Y and W-135) polysaccharide diphtheria toxoid conjugate vaccine / Menactra / Sanofi Pasteur	Use as a booster vaccination against meningococcal disease in people 15 to 55 years of age	[9/3/14]
Enalapril Maleate Powder for Oral Solution / Epaned / Silvergate Pharmaceuticals	Treatment of symptomatic heart failure and treatment of asymptomatic left ventricular dysfunction in patients older than one month of age	[9/4/14]
Enzalutamide / Xtandi / Astellas	First-line therapy for metastatic castration-resistant prostate cancer	[9/10/14]
Adalimumab / Humira / AbbVie	Use in pediatric Crohn's disease patients ages 6 years and older, when other treatments haven't worked, and treatment of polyarticular juvenile idiopathic arthritis in patients 2 to 4 years of age.	[9/23/14 & 9/30/14]
Estradiol transdermal system / Minivelle / Noven	Prevention of postmenopausal osteoporosis with new 0.025 mg/day patch	[9/23/14]
Apremilast / Otezla / Celgene	Treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy	[9/23/14]
Methylnaltrexone bromide / Reslistor / Salix Pharmaceuticals	Treatment of opioid-induced constipation in patients with chronic non-cancer pain	[9/29/14]

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Tiotropium bromide inhalation spray / Spiriva Respimat / Boehringer Ingelheim	Metered dose Respimat inhaler delivering a liquid mist from a spring-loaded actuator	[9/24/14]
Cobicistat / Tybost / Gilead	Tablet: 150 mg; to increase systemic exposure of atazanavir or darunavir in a combination regimen in the treatment of HIV-1 infection	[9/24/14]
Elvitegravir / Vitekta / Gilead	Tablet 85 mg; use with an HIV protease inhibitor coadministered with ritonavir in a combination regimen, for the treatment of HIV-1 infection in antiretroviral treatment-experienced adults	[9/24/14]
Fluocinolone acetonide intravitreal insert/ Iluvien / Alimera Sciences	Treatment of diabetic macular edema in patients previously treated with corticosteroids without a clinically important rise in intraocular pressure	[9/26/14]
Colchicine / Mitigare / Hikma Pharms	Capsules: 0.6 mg; prophylaxis of gout flares in adults	[9/26/14]

Compiled by:

Terri Levien, Pharm.D.
Ross Bindler, Pharm.D., PGY1 Drug Information Resident
Anne Kim, Pharm.D., PGY1 Drug Information Resident
Sarah Andrews, Pharm.D. Candidate 2015
Hue Thai, Pharm.D. Candidate 2015
Delaney Berggren, Pharm.D. Candidate 2015
Michael Huttula, Pharm.D. Candidate 2015
Alex Palmer, Pharm.D. Candidate 2015

Drug Information Center
College of Pharmacy
Washington State University
PO Box 1495
Spokane, WA 99210-1495
(509) 358-7662
Pharmacy.druginfo@wsu.edu

Pembrolizumab / Keytruda / Merck & Co.	
Generic Name / Brand Name / Company	Pembrolizumab / Keytruda / Merck & Co.
Date of approval	September 4, 2014
Drug Class (Mechanism of Action if novel agent)	Immunomodulator, monoclonal antibody that blocks the programmed death receptor-1 (PD-1).
Indication	Unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	For injection: 50 mg lyophilized powder in a single-use vial for reconstitution. Common dose: 2 mg/kg IV infusion over 30 minutes every 3 weeks – continue treatment until disease progression or unacceptable toxicity occurs.
DEA Schedule	Not applicable
Date of market availability	Anticipated availability is late September 2014.
Similar Medications (Look-Alike Sound-Alike)	Palivizumab, panitumumab
CLINICAL USE EVALUATION	
Common Adverse Effects	Pruritus, rash, constipation, decrease in appetite, diarrhea, nausea, arthralgia, cough, fatigue.
Severe Adverse Effects	Erythroderma, adrenal insufficiency, hypophysitis, anemia, hemolytic anemia, hepatitis, pancreatitis, Eaton-Lambert syndrome, rhabdomyolysis, optic neuritis, uveitis, nephritis, renal failure, pneumonitis, sepsis.
Severe Drug-Drug Interactions	No formal pharmacokinetic drug interaction studies have been conducted.
Severe Drug-Food Interactions	No studies have been conducted.
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Monitor for changes in liver, kidney, and thyroid function.
Used in Pediatric Areas	Safety and effectiveness have not been established in pediatric patients.
Renal or Hepatic Dosing	No dose adjustment needed in renal impairment. No dose adjustment needed for mild hepatic impairment [total bilirubin (TB) $\leq$ ULN and AST > ULN or TB > 1-1.5 times ULN and any AST]. No studies available for patients with moderate or severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No labeled contraindications. Cautions: immune-mediated adverse events including pneumonitis, colitis, hepatitis, hypophysitis, nephritis, hyperthyroidism, and hypothyroidism. Consider administration of corticosteroids. Embryofetal toxicity. Advise use of highly effective contraception during treatment and for 4 months after the last dose.
Special administration technique or considerations	Do not shake product, do not infuse with other medications. Infuse over 30 minutes through an IV line containing a sterile, non-pyrogenic, low-protein binding 0.2-5 micron filter.
Prepared by	Alex Palmer, PharmD. Candidate 2015

Ferric Citrate / Keryx Biopharmaceuticals	
Generic Name / Brand Name / Company	Ferric Citrate / Keryx Biopharmaceuticals
Date of approval	September 5, 2014
Drug Class (Mechanism of Action if novel agent)	Phosphate binder
Indication	Control of serum phosphate levels in patients with chronic kidney disease on dialysis
Comparative agent – Therapeutic interchange?	Sevelamer hydrochloride, calcium acetate, lanthanum
Dosage forms/strengths. Common Dose/sig	Tablet: 210 mg ferric iron, equivalent to 1 g ferric citrate Starting dose: 2 tablets orally TID with meals Titrate by 1 to 2 tablets per day as needed according to phosphate levels Max: 12 tablets/day
DEA Schedule	Not applicable
Date of market availability	Anticipated availability late 2014
Similar Medications (Look-Alike Sound-Alike)	Ferric Gluconate
CLINICAL USE EVALUATION	
Common Adverse Effects	Diarrhea, discolored feces, constipation, nausea, vomiting
Severe Adverse Effects	None reported
Severe Drug-Drug Interactions	Doxycycline: Take at least 1 hour before ferric citrate
Severe Drug-Food Interactions	No studies have been conducted
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Dose is titrated based on phosphate levels
Used in Pediatric Areas	Safety and efficacy has not been established in pediatric patients
Renal or Hepatic Dosing	None reported
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: Patients with iron overload syndromes Warnings: Iron overload, accidental iron overdose Not studied in patients with gastrointestinal bleeding or inflammation
Special administration technique or considerations	Take as directed with meals.
Prepared by	Delaney Berggren, PharmD Candidate 2015

Naltrexone SR & Bupropion SR Combination / Contrave / Orexigen Therapeutics, Inc.	
Generic Name / Brand Name / Company	Naltrexone SR & Bupropion SR Combination / Contrave / Orexigen Therapeutics, Inc.
Date of approval	September 11, 2014
Drug Class (Mechanism of Action if novel agent)	Combination opioid antagonist (naltrexone) and aminoketone antidepressant (bupropion)
Indication	Adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with initial BMI of: • 30 kg/m^2 or greater (obese) OR • 27 kg/m^2 or greater (overweight) with at least one weight-related comorbidity (e.g. hypertension, type 2 diabetes mellitus, dyslipidemia)
Comparative agent – Therapeutic interchange?	Belviq (lorcaserin HCl), Qsymia (phentermine and topiramate)
Dosage forms/strengths. Common Dose/sig	Extended-Release tablets: 8 mg naltrexone HCl/90 mg bupropion HCl • Week 1: 1 tablet QAM • Week 2: 1 tablet QAM, 1 tablet every evening • Week 3: 2 tablets QAM, 1 tablet every evening • Week 4- Onward: 2 tablets twice daily, morning and evening
DEA Schedule	Not applicable
Date of market availability	Fall 2014
Similar Medications (Look-Alike Sound-Alike)	Buprenorphine/Naloxone (Suboxone)

CLINICAL USE EVALUATION (Naltrexone SR & Bupropion SR Combination continued)	
Common Adverse Effects	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth and diarrhea
Severe Adverse Effects	Suicidal thoughts and behaviors; neuropsychiatric symptoms; seizures; increases in blood pressure or heart rate
Severe Drug-Drug Interactions	MAOIs, opioid analgesics, drugs that lower the seizure threshold (antipsychotics, antidepressants), CYP2D6-metabolized drugs (SSRIs, antipsychotics, beta-blockers, type 1C antiarrhythmic), CYP2D6 inhibitors
Severe Drug-Food Interactions	Avoid coadministration with high-fat meal.
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Monitor blood glucose in patients with diabetes; monitor blood pressure and heart rate in all patients.
Used in Pediatric Areas	Safety and effectiveness in pediatric patients (below 18) have not been established – use is not recommended in pediatric patients.
Renal or Hepatic Dosing	Renal impairment • Moderate to severe: Max daily dose is two tablets (one tablet each morning and evening). • Not recommended in end-stage renal disease Hepatic impairment: • Max recommended daily dose is one tablet in the morning
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: uncontrolled hypertension, seizure disorder or history of seizures, anorexia nervosa or bulimia, use of other bupropion-containing products, chronic opioid or opiate use, patients undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs, hypersensitivity to any product ingredients, pregnancy. Cautions: suicidal behavior and ideation, increases in blood pressure and heart rate, hepatotoxicity, angle-closure glaucoma.
Special administration technique or considerations	Tablets should not be cut, crushed, or chewed. Avoid administration with a high-fat meal.
Prepared by	Mike Huttula, PharmD Candidate, 2015

Naloxegol / Movantik / AstraZeneca	
Generic Name / Brand Name / Company	Naloxegol / Movantik / AstraZeneca
Date of approval	September 16, 2014
Drug Class (Mechanism of Action if novel agent)	Opioid antagonist
Indication	Opioid-induced constipation in patients with chronic non-cancer pain
Comparative agent – Therapeutic interchange?	Methylnaltrexone (Relistor)
Dosage forms/strengths. Common Dose/sig	Tablets: 12.5 mg, 25 mg Recommended dose: 25 mg orally once daily in the morning; reduce to 12.5 mg orally once daily if not tolerated.
DEA Schedule	Schedule II (DEA currently reevaluating)
Date of market availability	Anticipated availability in first half of 2015
Similar Medications (Look-Alike Sound-Alike)	Naloxone
CLINICAL USE EVALUATION	
Common Adverse Effects	Abdominal pain, diarrhea, flatulence, nausea, vomiting, headache.
Severe Adverse Effects	GI perforation, withdrawal signs or symptoms.
Severe Drug-Drug Interactions	Moderate and strong CYP3A4 inhibitors; other opioid antagonists
Severe Drug-Food Interactions	Grapefruit products
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	None
Used in Pediatric Areas	Safety and efficacy not established in pediatric patients.

Naloxegol continued…	
Renal or Hepatic Dosing	CrCl < 60mL/min: Adjust to 12.5 mg once daily; if tolerated, may increase to 25 mg daily. Avoid use in severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: known or suspected GI obstruction, concomitant use with strong CYP3A4 inhibitors. Cautions: gastrointestinal perforation, opioid withdrawal
Special administration technique or considerations	Take on an empty stomach and swallow whole; avoid consumption with grapefruit.
Prepared by	Alex Palmer, PharmD. Candidate 2015

Dulaglutide / Trulicity / Eli Lilly	
Generic Name / Brand Name / Company	Dulaglutide / Trulicity / Eli Lilly
Date of approval	September 19, 2014
Drug Class (Mechanism of Action if novel agent)	GLP-1 receptor agonist
Indication	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
Comparative agent – Therapeutic interchange?	Albiglutide, exenatide, liraglutide,
Dosage forms/strengths. Common Dose/sig	Injection: 0.75 mg/0.5 mL, 1.5 mg/0.5 mL in single dose pen or single-dose prefilled syringe Initiate 0.75 mg subcutaneously once weekly. Dose can be increased to 1.5 mg once weekly.
DEA Schedule	Not applicable
Date of market availability	Late 2014
Similar Medications (Look-Alike Sound-Alike)	
CLINICAL USE EVALUATION	
Common Adverse Effects	Nausea, diarrhea, vomiting, abdominal pain, decreased appetite
Severe Adverse Effects	Hypoglycemia
Severe Drug-Drug Interactions	Dulaglutide slows gastric emptying and has the potential to reduce the rate of absorption of concomitantly administered oral medications.
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Blood glucose, HbA1c
Used in Pediatric Areas	Not studied in this population
Renal or Hepatic Dosing	Renal: no dosage adjustment recommended. Monitor renal function in patients with renal impairment reporting severe GI reactions
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: Patients with a personal or family history of medullary thyroid carcinoma and in patients with Multiple Endocrine Neoplasia syndrome type 2 Warnings: Thyroid C-cell tumors (boxed warning – causes thyroid C-cell tumors in rats including medullary thyroid carcinoma), pancreatitis, hypoglycemia, hypersensitivity reactions, renal impairment
Special administration technique or considerations	Administer subcutaneously in the abdomen, thigh, or upper arm
Prepared by	Delaney Berggren, PharmD candidate 2014