Highlights of FDA Activities – 10/1/14 – 10/31/14

FDA Drug Safety Communications & Drug Information Updates:

FDA Alerts Health Care Providers and Emergency Responders of Expiration Date Extensions of Certain Auto-Injectors Manufactured by Meridian Medical Technologies – Drug Information Update [10/24/14]
Specific lots of AtroPen (atropine), CANA (diazepam), morphine sulfate, and pralidoxime chloride auto-injectors manufactured by Meridian Medical Technologies have had their expiration dates extended, allowing use for up to one additional year beyond the manufacturer's labeled expiration date. The complete list of products can be found in the link at: http://www.fda.gov/Drugs/DrugSafety/ucm376367.htm

Major Product Recalls Announced Through MedWatch:

Ketorolac Tromethamine Injection 30 mg/mL (Sagent): Recall – Incorrect expiration dates [10/06/14]
Ketorolac Tromethamine Injection, USP, 30 mg/mL (NDC 25021-701-01 and 25021-701-02) manufactured by Cadila Healthcare Limited and distributed by Sagent is being recalled due to incorrect expiration dates. Lot numbers being recalled are MP5021, MP5024, and MP5025 which were distributed nationwide September 17, 2014 through October 1, 2014. The labeled expiration date is longer than the known stability of the product.

Hudson RCI Pediatric Anesthesia Breathing Circuits by Teleflex Medical: Recall – Circuit Ends May Crack or Break [10/07/14]
Circuit used to deliver gases from a mechanical ventilator to pediatric patients may crack or break before or during use.

Vancomycin HCl for Injection 1 G (Hospira): Recall – Uncontrolled Storage During Transit [10/08/14]
Vancomycin HCl for Injection USP, equivalent to 1 G Vancomycin (Sterile Powder) from Hospira (NDC 0409-6533-01, Lot 35-315-DD with expiration date of 01 Nov 2015) recalled due to uncontrolled storage during transit. The product may have experienced temperature excursions during shipment to a customer and then was further distributed by the customer.

Junctional Tourniquet accessory (SAM Medical Products): Recall – Potential Clip Failure [10/08/14]
SAM Junctional tourniquet accessory (axilla) strap is being recalled because of potential clip failure. SAM Medical Products is arranging to rapidly replace the current axilla straps with an updated version.

ICU Medical ConMed Stat2 Flow Controller: Recall – Delivers Higher Flow Rate than Intended [10/10/14]
ConMed Stat2 Flow Controller has been recalled because it was assembled with the wrong internal component. The Flow Controller may deliver IV fluids at a much higher flow rate than what is set. The recalled item numbers are: 011-C9801, 011-C9802, AH7007, B9897, and Z2648.

CareFusion EnVe and ReVel Ventilators: Recall – Power Connection Failure [10/10/14]
EnVe and ReVel ventilators have been recalled because of potential for damage to their power cord adaptors which can cause loss of power and complete shut off. The firm recalled these devices because they found that the pins of the external power connector did not always align properly with the input port of the ventilator. A short circuit in the power supply may prevent the ventilator battery from recharging, and it could lose power unexpectedly. There have been 256 reports of the incident with no injuries or deaths.

Oregon Compounding Centers, Inc. Unexpired Sterile Products: Recall – Lack of Sterility Assurance [10/10/14]
Oregon Compounding Centers, Inc., also called Creative Compounds, is voluntarily recalling certain unexpired human and veterinary sterile products to the consumer level due to lack of sterility assurance. There have been no reports of product contamination or adverse events to date, but a recent inspection identified an issue with sterility

assurance. All recalled products have a label that includes the Creative Compounds name as well as a lot number, were made from July 1, 2014 through September 22, 2014, and were distributed in Oregon and Washington. A complete list of recalled products can be found in a link on the MedWatch site.

Medi-Trace Cadence and Kendall Multi-function Defibrillation Electrodes by Covidien: Field Safety Alert – Electrodes Will Not Connect with Philips FR3 or FRx AED Unit [10/12/14]
Covidien has alerted customers of a connector compatibility issue resulting from a mismatch between the Covidien electrodes and Philips FR3 and FRx defibrillators. The Philips AED units should only be used with Philips brand electrodes. Facilities should assure that Covidien electrodes have not been placed for use with Philips AEDs.

LifeCare Flexible Intravenous Solutions by Hospira, Inc.: Recall – Potential for Leakage [10/15/14]
Hospira is recalling certain lots of products in its LifeCare line of flexible intravenous solutions due to the potential for leakage. A completed list of recalled lots can be found in a link on the MedWatch site.

Lidocaine HCl Injection, USP 10 mg Per mL, 30 mL Single-Dose, Preservative-Free, by Hospira: Recall – Particulate Matter [10/17/14]
One lot of 1% Lidocaine HCl for injection, USP, 10 mg per mL, 30 mL Single-dose, Preservative-free from Hospira recalled due to a confirmed customer report of particulate in a single unit. The particulate has been identified as human hair, embedded in and attached to a pinched area of the stopper. Lot affected: NDC 0409-4279-02; Lot 40-316-DK, Expiry 1APRIL2016. Distributed from May 2014 through June 2014.

Saba Shark Cartilage Complex, 60 Capsule Bottles: Recall – Possible Salmonella Contamination [10/20/14]
AMS Health Sciences, LLC is recalling 2014 bottles of Saba Shark Cartilage Complex due to possible contamination of Salmonella. Product affected: Lot Number 416349 with an expiration date of 08/16, sold to customers during the period of February through August 2014.

Assured Brand Naproxen Sodium Tablets by Contract Packaging Resources, Inc.: Recall – Packaging Mix-up [10/22/14]
Contract Packaging Resources, a drug repackaging company, is voluntarily recalling 11,640 boxes of Assured brand Naproxen Sodium because some cartons actually contain bottles of Ibuprofen. Affected products: Boxes of Assured brand Naproxen Sodium Tablets 220mg, 15 count (Lot #FH4102A) containing bottles of Ibuprofen softgels in 200mg strength. The recalled Assured brand products were distributed via the Dollar Tree retail stores and internet site

Intravia Containers by Baxter: Recall - Particulate Matter [10/25/14]
Baxter International Inc. is recalling two lots of INTRAVIA containers due to complaints of particulate matter found inside the fluid path. Recalled lots are INTRAVIA Container, 150 mL Capacity, Lot Number UR13D15112, Product Code 2B8011, distributed to customers between April 26, 2013 and June 20, 2013; and INTRAVIA Container, Empty 500 mL Capacity, Lot Number UR13K14095, Product Code 2B8013, distributed to customers between November 27, 2013 and March 10, 2014.

Baby Wipes by Nutek Disposables, Inc.: Recall - May Contain Bacteria [10/27/14]
Nutek Disposables, Inc is voluntarily recalling all lots of baby wipes that it manufactured under the brand names Cuties, Diapers.com, Femtex, Fred's, Kidgets, Member's Mark, Simply Right, Sunny Smiles, Tender Touch, and Well Beginnings, because some packages may contain the bacteria *Burkholderia cepacia*. These wipes were distributed by Nutek prior to October 21, 2014 to the following retail stores: Walgreens, Sam's Club, Family Dollar, Fred's, and Diapers.com.

10 Percent Neutral Buffered Formalin by Richard-Allan Scientific: Class I Recall - May Contain Incorrect Concentration of Formalin [10/31/14]
Richard-Allan Scientific is recalling 10 percent Neutral Buffered Formalin manufactured on July 18, 2014 and distributed from July 18 to September 17, 2014. Defective products returned from several customers were found to have from 0 percent to 3 percent Formalin content instead of the required 10 percent. A too-low or too high concentration of Formalin will not properly preserve or can damage tissues.

Dietary Supplement Recalls & Public Notifications

In October, 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)***
Sit and Slim II	Weight loss	Sibutramine and phenolphthalein
Ginseng Kianpi Pil	Promote weight gain & relieve fatigue	Dexamethasone and cyproheptadine

New Product Shortages Reported by the FDA:	***Date Initially Posted***
Dextrose Injection USP, 70%	[10/03/14]
Triamcinolone Hexacetonide Injection Suspension	[10/03/14]
Azathioprine 50 mg Tablets	[10/06/14]
Radium RA-223 Dichloride (Xofigo) Injection	[10/07/14]
Technetium Tc99m Succimer Injection (DMSA)	[10/15/14]

Product Discontinuations/Withdrawals	***Date Initially Posted***
Desogestrel and Ethinyl Estradiol tablets (Ortho-Cept) will be discontinued by Janssen Pharmaceuticals; last distribution will be March 2015; generics remain available.	[10/08/14]
Chlorzoxazone 500 mg Caplets (Parafon Forte DSC) is being discontinued by Janssen; generics remain available.	[10/16/14]
Norelgestromin/Ethinyl Estradiol Transdermal System (Ortho Evra) is being discontinued by Janssen Pharmaceuticals; Xulane, the Mylan branded generic remains available.	[10/21/14]

New Drug Approvals:	***Description***	***Date Approved***
Akynzeo / netupitant and palonosetron / Eisai Inc.	See attached drug summary	[10/10/14]
Harvoni / ledipasvir and sofosbuvir / Gilead	See attached drug summary	[10/10/14]
Lumason / Sulfur hexafluoride lipid-type A microspheres injectable suspension / Bracco	Imaging agent for use in patients with suboptimal echocardiograms to opacify the left ventricular chamber and improve delineation of the left ventricular endocardial border.	[10/10/14]
Esbriet / pirfenidone / InterMune, Inc.	See attached drug summary	[10/15/14]
Ofev / nintedanib / Boehringer Ingelheim Pharmaceuticals, Inc.	See attached drug summary	[10/15/14]
Obizur/ antihemophilic factor (recombinant), porcine sequence/ Baxter International Inc.	Antihemophilic factor indicated for the treatment of bleeding episodes in adults with acquired hemophilia A.	[10/23/14]
Trumenba / Meningococcal group B vaccine / Wyeth Pharmaceuticals	Immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B. Approved for use in individuals 10 through 25 years of age. Three dose series administered on a 0-, 2-, and 6-month schedule.	[10/29/14]

New Indications:	***Description***	***Date Approved***
Aflibercept injection / Eylea / Regeneron	Treatment of macular edema following retinal vein occlusion.	[10/06/14]
Bortezomib for injection / Velcade / Millennium Pharmaceuticals	Treatment of mantle cell lymphoma in previously untreated patients.	[10/08/14]

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Budesonide 2 mg rectal foam / Uceris / Salix	For the induction of remission in patients with active mild-to-moderate ulcerative colitis extending up to 40 cm from the anal verge.	[10/07/14]
Sotalol HCl oral solution / Sotylize / Arbor	For the treatment of documented life-threatening ventricular arrhythmias and the maintenance of normal sinus rhythm in patients with a history of highly symptomatic atrial fibrillation/flutter.	[10/23/14]
Dapagliflozin & metformin HCl / Xigduo XR / AstraZeneca	Extended-release combination tablet containing dapagliflozin 5 mg or 10 mg & metformin 500 mg or 1000 mg to be administered once daily in the morning to improve glycemic control in adults with type 2 diabetes mellitus.	[10/29/14]

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Netupitant and Palonosetron / Akynzeo / Eisai Inc.	
Generic Name / Brand Name / Company	Netupitant and palonosetron / Akynzeo / Eisai Inc.
Date of approval	October 10, 2014
Drug Class (Mechanism of Action if novel agent)	Combination of a selective antagonist of human substance P/neurokinin 1 (NK_1) receptors and a 5-HT_3 receptor antagonist
Indication	Prevention of acute and delayed chemotherapy-induced nausea and vomiting
Comparative agent – Therapeutic interchange?	Aprepitant in conjunction with a 5-HT_3 receptor antagonist
Dosage forms/strengths. Common Dose/sig	Capsule: 300 mg netupitant/0.5 mg palonosetron Take 1 capsule one hour prior to the start of chemotherapy
DEA Schedule	Not applicable
Date of market availability	Currently unknown
Similar Medications (Look-Alike Sound-Alike)	Palonosetron
CLINICAL USE EVALUATION	
Common Adverse Effects	Headache, asthenia, dyspepsia, fatigue, constipation, and erythema
Severe Adverse Effects	Anaphylaxis, serotonin syndrome
Severe Drug-Drug Interactions	CYP3A4 substrates, inducers, and inhibitors; serotonergic drugs
Severe Drug-Food Interactions	Grapefruit
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 effectiveness not established in patients under 18 years
Renal or Hepatic Dosing	Avoid use in patients with severe hepatic or renal impairment
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: none Warnings: hypersensitivity reactions (including anaphylaxis) have been reported; serotonin syndrome, especially with concomitant use of serotonergic drugs
Special administration technique or considerations	Administer along with dexamethasone at a dexamethasone dose indicated for the type of chemotherapy
Prepared by	Alex Palmer, Pharm.D. Candidate 2015

Ledipasvir and Sofosbuvir / Harvoni / Gilead	
Generic Name / Brand Name / Company	Ledipasvir and sofosbuvir / Harvoni / Gilead
Date of approval	October 10, 2104
Drug Class (Mechanism of Action if novel agent)	Combination NS5A inhibitor (ledipasvir) and NS5B polymerase inhibitor (sofosbuvir)
Indication	Treatment of chronic hepatitis C (genotype 1) infection
Comparative agent – Therapeutic interchange?	sofosbuvir in combination with simeprevir
Dosage forms/strengths. Common Dose/sig	Tablet: ledipasvir 90 mg and sofosbuvir 400 mg Dose: 1 tablet orally once daily Duration: Without cirrhosis (treatment naïve or experienced) – 12 weeks** With cirrhosis (treatment naïve)—12 weeks With cirrhosis (treatment experienced) – 24 weeks **8 week duration can be considered in treatment-naïve **without** cirrhosis if pre-treatment HCV RNA <6 million IU/mL
DEA Schedule	Not applicable
Date of market availability	Fall 2014
Similar Medications (Look-Alike Sound-Alike)	Sofosbuvir
CLINICAL USE EVALUATION	
Common Adverse Effects	Fatigue, headache, nausea, diarrhea, insomnia; fatigue and headache incidence greater than 10%.
Severe Adverse Effects	Rare
Severe Drug-Drug Interactions	- Ledipasvir and sofosbuvir are P-gp inhibitors and substrates (rifampin and St. John's Wort may ↓ Harvoni levels) - Acid-reducing agents (PPIs, H_2 RAs, aluminum/magnesium) ↓ ledipasvir levels - Anticonvulsants (carbamazepine, oxcarbazepine, phenytoin) ↓ levels of both ledipasvir and sofosbuvir - HIV-Related: Tenofovir levels ↑ (avoid combination)
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	HCV viral load
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	Renal: No adjustment in mild-to-moderate impairment; no data for severe (<30 mL/min GFR) Hepatic: No dosage adjustment in mild, moderate or severe (Child-Pugh Class A, B, or C); safety/efficacy not established in decompensated cirrhosis
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No contraindications in labeling; co-administration with P-glycoprotein inducers (eg. Rifampin, St. John's Wort) or sofosbuvir not recommended.
Special administration technique or considerations	Administer for full treatment duration (8, 12, or 24 weeks) based on previous treatment status, disease progression and HCV viral load. May be administered with or without food.
Prepared by	Mike Huttula, PharmD Candidate 2015

Pirfenidone / Esbriet / InterMune, Inc.	
Generic Name / Brand Name / Company	Pirfenidone / Esbriet / InterMune, Inc.
Date of approval	October 15, 2014
Drug Class (Mechanism of Action if novel agent)	Anti-fibrotic/anti-inflammatory agent: Precise MOA unknown, however it may decrease fibroblast proliferation and production of fibrosis-associated proteins and cytokines, along with decreasing formation and accumulation of extracellular matrix in response to transforming growth factor-beta and platelet derived growth factor.
Indication	Treatment of idiopathic pulmonary fibrosis
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Capsule: 267 mg Days 1-7: one capsules three times daily with meals Days 8-14: two capsules three times daily with meals Day 15 and thereafter: three capsules three times daily with meals
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Easprin, perphenazine
CLINICAL USE EVALUATION	
Common Adverse Effects	Nausea, rash, abdominal pain, upper respiratory tract infection, diarrhea, fatigue, headache, dyspepsia, dizziness, vomiting, anorexia, gastro-esophageal reflux disease, sinusitis, insomnia, weight decreased, arthralgia
Severe Adverse Effects	Photosensitivity, rash, elevated liver enzymes or bilirubin
Severe Drug-Drug Interactions	Avoid with strong CYP1A2 inhibitors or inducers; dosage reductions with moderate CYP1A2 inhibitors; avoid with agents that are moderate or strong inhibitors of CYP1A2 and one or more other CYP pathways.
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Liver function tests prior to initiation, then monthly for the first 6 months, and every 3 months thereafter
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	Monitor for adverse reactions and consider dose modification or discontinuation for patients with mild to moderate hepatic or renal impairment. Avoid use in severe hepatic impairment or severe renal impairment requiring dialysis.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No labeled contraindications. Drug interactions with CYP1A2 inhibitors or inducers. Smoking reduces exposure to pirfenidone; patients should stop smoking prior to initiation of therapy. Precautions: exposure to sunlight may result in rash; dosage adjustments or discontinuation may be necessary in patients with elevated liver enzymes or bilirubin, photosensitivity or rash, or gastrointestinal disorders.
Special administration technique or considerations	Take with food to decrease nausea and dizziness
Prepared by	Alex Palmer, Pharm.D. Candidate 2015

Nintedanib / Ofev / Boehringer Ingelheim Pharmaceuticals, Inc.	
Generic Name / Brand Name / Company	Nintedanib / Ofev / Boehringer Ingelheim Pharmaceuticals, Inc.
Date of approval	October 15, 2014
Drug Class (Mechanism of Action if novel agent)	Tyrosine kinase inhibitor
Indication	Treatment of idiopathic pulmonary fibrosis
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Capsules: 100 mg and 150 mg Recommended dosage: 150 mg twice daily taken 12 hours apart, consider temporary dose reduction to 100 mg twice daily for management of adverse reactions
DEA Schedule	Not applicable
Date of market availability	Available
CLINICAL USE EVALUATION	
Common Adverse Effects	Diarrhea, nausea, abdominal pain, liver enzyme elevation, vomiting, decreased appetite, weight decrease, headache, hypertension
Severe Adverse Effects	Bronchitis, myocardial infarction, pneumonia, lung neoplasm malignant
Severe Drug-Drug Interactions	Concomitant use of potent P-glycoprotein and CYP3A4 inhibitors may increase exposure to nintedanib Concomitant use of potent P-glycoprotein and CYP3A4 inducers may decrease exposure to nintedanib May increase risk of bleeding if patient is taking anticoagulant
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Monitor liver function tests (ALT, AST and bilirubin) before initiating treatment, monthly for 3 months, and every 3 months thereafter
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	Hepatic impairment: Monitor for adverse reactions and consider dose modification or discontinuation for patients with mild impairment; avoid use in moderate or severe hepatic impairment. Renal impairment: The safety and efficacy have not been studied in patients with severe renal impairment and end-stage renal disease
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No labeled contraindications. Monitor for elevated liver enzymes Gastrointestinal disorders: Discontinue if severe diarrhea, nausea or vomiting persists despite symptomatic treatment Embryofetal toxicity: Woman of childbearing potential should be advised of the potential hazard to the fetus and avoid becoming pregnant Arterial thromboembolic events: Use caution when treating patients at high cardiovascular risk Bleeding: Use in patients with known bleeding risk only if benefit outweighs the potential risk Gastrointestinal perforation: Use with caution in patients with recent abdominal surgery Smoking reduces exposure to nintedanib; patients should stop smoking prior to initiation of therapy.
Special administration technique or considerations	Take capsules with food; swallow capsules whole with liquid
Prepared by	Delaney Berggren, Pharm.D. Candidate 2015