Highlights of FDA Activities – 12/1/2016 – 12/31/2016

FDA Drug Safety Communications & Drug Information Updates:

Pioglitazone: Drug Safety Communication – Increased Risk of Bladder Cancer 12/12/16
The FDA has concluded that pioglitazone may be linked to an increased risk of bladder cancer. The labels of all pioglitazone-containing medications are being updated to describe the additional studies reviewed along with the warnings regarding the risks of using any pioglitazone containing product.

General Anesthetic and Sedation Drugs: Drug Safety Communication – New Warnings for Young Children and Pregnant Women 12/14/16
The FDA warned that the repeated and lengthy use of general anesthetics and sedation drugs during procedures in children younger than 3 years old or in pregnant women during their third trimester may affect the development of the child's brain.

Chantix (varenicline) and Zyban (bupropion): Drug Safety Communication - Mental Health Side Effect Labeling Revised 12/16/16
The FDA is removing the boxed warning for serious mental health side effects from Chantix (varenicline) and Zyban (bupropion) drug labels following determination that the risk of serious side effects on mood, behavior, or thinking with the stop-smoking medicines Chantix and Zyban is lower than previously suspected. The FDA will be updating the existing warning sections in both labels that describes the side effects on mood, behavior, or thinking to include the results from the clinical trial. Although risks are still present, especially in those with mental illness or a history of mental illness, the latest study results suggest the benefits of quitting smoking are greater than the risks associated with the use of these agents.

Clozapine Risk Evaluation and Mitigation Strategy (REMS) Program Update 12/19/16
The FDA announced that the December launch of the clozapine REMS program would not be implemented in 2016 due to technical challenges. During postponement, the FDA and Clozapine Product Manufacturers' Group will ensure that patients have access to clozapine and appropriately supervise its safe use during the transition to a fully implemented clozapine REMS Program. Prescribers and pharmacies are encouraged to use this additional time to certify in the clozapine REMS program before the full launch.

Major Product Recalls Announced Through MedWatch:

Medtronic Neurovascular Products: Recall – Potential Separation and Detachment of Coating 12/1/16
Certain lots of Medtronic Pipeline™ Embolization device, Alligator™ Retrieval device, X-Celerator™ hydrophilic guidewires, and UltraFlow™/Marathon™ flow-directed micro catheters used in the treatment of cerebral aneurysm are being recalled due to the potential separation and detachment of the polytetrafluoroethylene (PTFE) coating on parts of these devices. A complete list of recalled lot numbers can be found on MedWatch.

Centurion Multi-Med Single Lumen Catheters: Recall – Excess Material May Split or Separate 12/9/16
Centurion Convenience Kits containing Multi-Med Single Lumen Catheters distributed from 5/23/16 to 10/18/16 recalled due to potential for excess material in the catheter tip to separate from the catheter and enter the patient's bloodstream. A complete list of recalled Kit Codes and Lot Numbers can be found on MedWatch.

Standard Offset Cup Impactor with POM-C Handle by Greatbatch Medical: Class I Recall - Inadequate Sterilization 12/20/16
Greatbatch Medical recalled the Standard Offset Cup Impactor with a POM-C handle, a device used during hip joint replacement surgeries, following failed sterility testing. A complete list of recalled model numbers can be found on MedWatch.

Dietary Supplement Recalls & Public Notifications

In December, the FDA issued notifications to the public regarding undeclared active ingredients in the following product. Patients are advised not to purchase or use this product.

Product	*Promoted Use*	*Hidden/Undeclared Drug Ingredient(s)*
90° Jiushidu	Sexual-enhancement	Sildenafil[1]
African Viagra	Sexual-enhancement	Sildenafil[1]
Big Penis Male Sexual Stimulant	Sexual enhancement	Sildenafil[1]
Bl4ck 4K Capsules	Sexual enhancement	Sildenafil[1]
Black 3K Plus	Sexual enhancement	Sildenafil[1]
Black Mamba 2 Premium	Sexual enhancement	Sildenafil[1]
Duramaxxx	Sexual-enhancement	Sildenafil[1]
Lang Yi Hao	Sexual-enhancement	Sildenafil[1]
Megajex Natural Male Sex Enhancer*	Sexual enhancement	Sildenafil[1] and tadalafil[2]
Power Male Sexual Stimulant*	Sexual enhancement	Sildenafil[1]
Queen Slimming Soft Gel	Weight-loss	Sibutramine[3]
Rhino 5 1500 Capsules	Sexual enhancement	Sildenafil[1]
Rhino 7K 9000 Male Performance Booster	Sexual enhancement	Sildenafil[1]
Rhino 8 Platinum 8000	Sexual enhancement	Sildenafil[1]
Rhino 9 Premium 3500	Sexual enhancement	Sildenafil[1]
Triple Green	Sexual-enhancement	Sildenafi[1]l
Ultimate Body Tox PRO*	Weight-loss	Sibutramine[3]

*Recalled

[1] Sildenafil taken unknowingly with nitrates may lower blood pressure to dangerously low levels

[2] Tadalafil taken unknowingly with nitrates may lower blood pressure to dangerously low levels

[3]Sibutramine: oral anorexiant; risk - increased cardiovascular events; discontinued 2010[FDA]

New Product Shortages Reported by the FDA:	*Date Initially Posted*
Ranitidine Injection, USP	12/8/16
Hydroxyamphetamine hydrobromide/tropicamide ophthalmic (Paremyd, Akorn)	12/9/16

Product Discontinuations/Withdrawals	*Date Posted*
Alendronate Sodium Tablets (Mylan Pharmaceuticals): Mylan Pharmaceuticals discontinued the manufacturing of 70 mg, 4s, (NDC: 0378-3569-99) and 35 mg, 4s, (NDC: 0378-3568-99); these alendronate tablet strengths remain available from other generic manufacturers	12/01/16
Naratriptan Tablets (Mylan Pharmaceuticals): Mylan-Pharmaceuticals discontinued the manufacturing of 2.5 mg, 9s (NDC: 0378-4451-59); naratriptan tablets remain available from other generic manufacturers	12/20/16
Tretinoin Cream (Tretin-X, Allergan): Allergan Sales LLC discontinued the manufacturing of 0.0375%, 2 gm (NDC: 16781-376-02), 0.0375%, 35 gm (NDC: 16781-376-35), 0.075%, 2 gm (NDC: 16781-446-35) and 0.075%,35 gm (NDC: 16781-446-35); alternative tretinoin cream products remain available	12/22/16
Etomidate injection (Amidate, Hospira Inc): Hospira Inc discontinued the manufacturing of 2 mg/mL; 40 mg/20 mL Glass Ampul (NDC: 0409-8061-01) and 2 mg/mL; 20 mg/10 mL Glass Ampul (NDC: 0409-8062-01); etomidate injection remains available from generic manufacturers	12/22/16

New Drug Approvals:	***Description***	***Date Approved***
Crisaborole ointment 2% / Eucrisa / Anacor Pharmaceuticals	Phosphodiesterase 4 inhibitor indicated for topical treatment of mild to moderate atopic dermatitis in patients 2 years of age and older – see attached drug summary	12/14/16
Rucaparib / Rubraca / Clovis Oncology	Poly (ADP-ribose) polymerase inhibitor for advanced ovarian cancer with tumors expressing deleterious BRCA gene mutation – see attached drug summary	12/19/16
Nusinersen / Spinraza / Biogen	Spinraza is a survival motor neuron-2 (SMN2)-directed antisense oligonucleotide indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients – see attached drug summary	12/23/16

New Indications:	***Description***	***Date Approved***
Empagliflozin / Jardiance / Boehringer Ingelheim Pharmaceuticals, Inc.	The FDA approved indication to reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and cardiovascular disease.	12/2/16
Bevacizumab / Avastin / Genentech	Ovarian cancer in patients with platinum-sensitive recurrent disease as part of a combination chemotherapy regimen followed by continued bevacizumab administration	12/6/16
Insulin degludec / Tresiba / Novo Nordisk	Indication expanded to include use to improve glycemic control in children as young as age 1 and adolescents with either type 1 or type 2 diabetes mellitus	12/16/16

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Empagliflozin and metformin HCl extended-release tablets / Synjardy XR / Boehringer Ingelheim	Extended-release tablet formution containing empagliflozin 25 mg and metformin HCl 2000 mg for once daily administration	12/9/16

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Crisaborole Ointment 2% / Eucrisa™ / Pfizer (Anacor Pharmaceuticals, Inc.)	
Generic Name / Brand Name / Company	Crisaborole ointment 2% / Eucrisa / Pfizer (Anacor Pharmaceuticals)
Date of approval	December 14, 2016
Drug Class (Mechanism of Action if novel agent)	Immunomodulators; Non-steroidal anti-inflammatory phosphodiesterase 4 (PDE-4) inhibitors
Indication	Treatment of mild to moderate eczema (atopic dermatitis) in patients two years of age and older

Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Topical ointment 2%, applied topically twice daily
DEA Schedule	Not scheduled
Date of market availability	January 2017
Similar Medications (Look-Alike Sound-Alike)	Crizotinib, Eucreas, Tavaborole
Clinical Use Evaluation	
Common Adverse Effects	Application-site pain (4.4%)
Severe Adverse Effects	Contact urticaria
Severe Drug-Drug Interactions	None reported
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry or at point of clinical follow up.	No laboratory monitoring required.
Used in Pediatric Areas	Crisaborole has not been studied in patients under 2 years of age
Renal or Hepatic Dosing	None
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Discontinue use if signs or symptoms of hypersensitivity occur (contact urticaria, severe pruritus, swelling or erythema at the application site or distant site)
Special administration technique or considerations	None
Prepared by	Alice Knotts, Pharm.D. student, Class of 2018
Source	Eucrisa (crisaborole) ointment 2% prescribing information. Palo Alto, CA: Anacor Pharmaceuticals, Inc. December 2016. FDA approves Pfizer ointment for chronic itchy skin conditions. Reuters Health News. www.reuters.com Updated December 14, 2016; Accessed January 3, 2017. (includes price and availability information)

Rucaparib / Rubraca / Clovis Oncology, Inc	
Generic Name / Brand Name / Company	Rucaparib / Rubraca / Clovis Oncology, Inc
Date of approval	December 19, 2016
Drug Class (Mechanism of Action if novel agent)	Poly (ADP-ribose) polymerase (PARP) inhibitor
Indication	Monotherapy treatment of patients with deleterious BRCA mutation associated advanced ovarian cancer who have been treated with two or more chemotherapies.
Comparative agent – Therapeutic interchange?	Olaparib
Dosage forms/strengths. Common Dose/sig	Tablets: 200 mg and 300 mg, Take 600 mg orally daily with or without food
DEA Schedule	Not scheduled
Date of market availability	Available through specialty limited distribution network
Similar Medications (Look-Alike Sound-Alike)	Prucalopride
Clinical Use Evaluation	
Common Adverse Effects	Nausea, fatigue, vomiting, anemia, abdominal pain, dysgeusia, constipation, decreased appetite, diarrhea, thrombocytopenia, and dyspnea
Severe Adverse Effects	Anemia, thrombocytopenia, neutropenia, myelodysplastic syndrome/ acute myeloid leukemia
Severe Drug-Drug Interactions	None reported
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?)	Complete blood count at baseline and monthly; creatinine, ALT, AST, hemoglobin as clinically indicated
Used in Pediatric Areas	Safety and effectiveness have not been established.
Renal or Hepatic Dosing	None; not studied in patients with severe renal impairment or moderate to severe hepatic impairment

Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Hematologic toxicity, myelodysplastic syndrome or acute myeloid leukemia – monitor Embryo-Fetal Toxicity Photosensitivity
Special administration technique or considerations	Take doses approximately 12 hours apart. If patient misses a dose or vomits after taking a dose, do not take an extra dose.
Prepared by	Uzoma Mbogu, Pharm.D. student, Class of 2018
Source	Rubraca (rucaparib) tablets prescribing information. Boulder, CO: Clovis Oncology, Inc. December 2016. FDA approves Rubraca for BRCA-mutated advanced ovarian cancer. FDA.gov website. Accessed December 19, 2016.

Nusinersen / Spinraza / Biogen	
Generic Name / Brand Name / Company	Nusinersen / Spinraza / Biogen
Date of approval	December 23, 2016
Drug Class (Mechanism of Action if novel agent)	Survival motor neuron-2 (SMN2)-directed antisense oligonucleotide
Indication	Spinal muscular atrophy (SMA) in pediatric and adult patients
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Injection: 12 mg/5 mL solution in a single dose glass vial 12 mg intrathecally, initiated with three doses at 14 day intervals, followed by a 4th dose at 30 days after the 3rd dose and then a dose every 4 months
DEA Schedule	Not Scheduled
Date of market availability	January 2017
Similar Medications (Look-Alike Sound-Alike)	Lovaza, Spinosad
Clinical Use Evaluation	
Common Adverse Effects	Headache (50%), lower respiratory tract infection (43%), backache (41%), reaction to lumbar puncture (41%), upper respiratory infection (39%), constipation (30%)
Severe Adverse Effects	Thrombocytopenia, hyponatremia, hematologic abnormalities, atelectasis, renal toxicity
Severe Drug-Drug Interactions	None reported
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?)	CBC, platelet count, aPTT, and quantitative spot urine protein at baseline and prior to each dose
Used in Pediatric Areas	Approved in pediatric patients
Renal or Hepatic Dosing	None
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Thrombocytopenia and coagulation abnormities: Increased risk for bleeding complications; testing required at baseline and before each dose Renal toxicity: Quantitative spot urine protein testing required at baseline and prior to each dose
Special administration technique or considerations	Intrathecal use only, consider sedation. May consider ultrasound or other imaging techniques to guide administration, particularly in younger patients. Prior to administration remove 5 mL of CSF. Administer nusinersen as a bolus over 1-3 minutes.
Prepared by	Tori DeMyer and Courtney Mayo, Pharm.D. students, Class of 2017
Source	Spinraza (nusinersen) injection prescribing information. Cambridge, MA: Biogen Inc.; December 2016.