Highlights of FDA Activities – 1/1/18 – 1/31/18

FDA Drug Safety Communications & Drug Information Updates:

Opioid Cough and Cold Medicines: Labeling Changes to Limit Use to Adults 1/11/18
The FDA is requiring safety labeling changes for prescription cough and cold medicines containing codeine or hydrocodone to limit the use of these products to adults 18 years and older and to add additional safety information about the risks of misuse, abuse, addiction, overdose, death, and slowed or difficult breathing to the Boxed Warning.

Becton-Dickinson Syringe Stoppers Replaced: Drug Information Update 1/12/18
The FDA announced that Becton-Dickinson had informed the agency that the manufacturer is no longer using the rubber stopper material that had been associated with loss of drug in its general use syringes. The company has returned to the rubber stopper material previously used. The FDA reminded health care professionals that general use BD syringes remain approved for immediate use in fluid aspiration and injection, but not for use as a closed container storage system for drug products. Suitability for that purpose has not been established for the syringes with either rubber stopper material

Rolapitant Injectable Emulsion (Varubi): Anaphylaxis and Other Serious Hypersensitivity Reactions 1/16/18
New safety information for rolapitant injectable emulsion was distributed through a health care provider letter describing anaphylaxis, anaphylactic shock and other serious hypersensitivity reactions that have been observed postmarketing. Most reactions have occurred within the first few minutes of administration. Healthcare professionals should be vigilant for hypersensitivity reactions and consult with patients prior to administration to determine if the patient is allergic to any product ingredients (including soybean oil) and to consider potential cross-reacting allergens such as legumes.

Illegal, Unapproved Opioid Cessation Products: Drug Information Update 1/24/18
The FDA and Federal Trade Commission posted warning letters to the marketers and distributers of 12 opioid cessation products for illegally marketing unapproved products using deceptive claims. The FDA/FTC joint warning letters were sent to 11 companies for their products: Opiate Freedom Center ("Opiate Freedom 5-Pack"), U4Life, LLC ("Mitadone"), CalmSupport, LLC ("CalmSupport"), TaperAid ("TaperAid" & "TaperAid Complete"), Medicus Holistic Alternatives LLC ("Natracet"), NutraCore Health Products, LLC ("Opiate Detox Pro"), Healthy Healing, LLC ("Withdrawal Support"), Soothedrawal, Inc. ("Soothedrawal"), Choice Detox Center, Inc. ("Nofeel"), GUNA, Inc. ("GUNA-ADDICT 1"), and King Bio, Inc. ("AddictaPlex"). An additional 4 letters were sent by the FTC. Additional information can be found on the FDA web site.

FDA Launches New REMS Webpages 1/29/18
To help with compliance and make locating information more efficient, the FDA has launched a new set of webpages for REMS and information about them. The page will have different sections for patients, health care providers and industry.

Imodium (loperamide) for Over-the-Counter Use: FDA Limits Packaging to Encourage Safe Use 1/30/18
The FDA is working with manufacturers to use blister packs or other single dose packaging for OTC loperamide and to limit the number of doses in a package. This effort is in response to reports of serious heart problems and deaths with use of much higher than recommended doses.

Major Medication or Pharmacy-Related Product Recalls Announced Through MedWatch:

Ampicillin and Sulbactam for Injection USP by Auromedics: Recall- Presence of Glass Particles 1/9/2018
AuroMedics Pharma LLC recalled lot AF0117001-A, Expiry date Dec 2018, of Ampicillin and Sulbactam for Injection USP, 1.5 g (equivalent to 1 g ampicillin as the sodium salt plus 0.5 g sulbactam as the sodium salt) in a single-dose vial, to the hospital level. The product has been found to contain glass particles. AuroMedics shipped the entire lot to wholesalers and/or hospitals nationwide on February 9, 2017.

Clopidogrel Tablets USP, 75 mg, by International Laboratories, LLC: Recall - Mislabeling 1/10/2018
International Laboratories, LLC recalled Lot# 117099A of Clopidogrel Tablets, USP 75 mg, packaged in bottles of 30 tablets (NDC 54458-888-16), to the consumer level due to mislabeling. The product is labeled as Clopidogrel tablets USP 75 mg but may contain Clopidogrel 75 mg or Simvastatin Tablets USP 10 mg. The product was distributed nationwide and delivered to distribution centers in Arkansas, Georgia, Indiana, California and Maryland, and distributed to retail stores in all US States.

Compounded Sterile Products by PharMEDium Services, LLC: Recall - Lack of Sterility Assurance 1/12/18
A limited recall initially announced on 12/27/17 was expanded on 1/11/18 to include all lots within expiry compounded at the Memphis, TN facility upon FDA request following a recent inspection. A complete list of all recalled products can be found on the MedWatch site.

Levofloxacin in 5% Dextrose 250 mg/50 mL for Injection by AuroMedics Pharma LLC: Recall- Presence of Visible Particulate Matter Tentatively Identified as Mold 1/18/18
AuroMedics Pharma LLC recalled one lot of Levofloxacin in 5% Dextrose Injection 250 mg/50 mL in a Single-Use flexible container NDC 55150-243-46, Lot CLF160003, Expiry date May 2018, to the hospital level. The product has been found to contain visible particulate matter tentatively identified as mold. AuroMedics shipped the lot to wholesalers and/or hospitals nationwide September 19 through October 31, 2017.

Basic Drugs Brand of Senna Laxative: Recall Due to Mislabeling 1/22/18
Magno-Humphries Laboratories, Inc., recalled one lot of Basic Drugs Brand of Senna Laxative tablets, 8.6 mg sennosides (Lot#352300, EXP: 01/19 printed on the bottom of the bottle) to the consumer level due to a customer complaint that their bottle labeled as Senna Laxative actually contained Basic Drugs Brand of Naproxen Sodium 220 mg. Basic Drugs Brand Senna Laxative tablets were distributed nationwide to secondary distributors, retail pharmacies and via the internet.

Multiple Drug Products by Flawless Beauty: Recall – Misbranded or Unapproved 1/22/18
Flawless Beauty, LLC recalled all lots of 19 different products alleged by the FDA to be misbranded or unapproved new drugs. All products were sold over the Internet, and include whitening kits containing the recalled glutathione, vitamin C or sterile water, as well as a Ling Zhi capsule. A complete list of products can be found on the FDA site.

Nexterone Injection from Baxter: Recall - Presence of Particulate Matter 1/23/18
Baxter International Inc. expanded the recall of Nexterone (amiodarone) injection to include a second lot (NC109123) due to the potential presence of particulate matter. The additional lot was distributed between 7/21/17 and 10/2/17 to wholesalers/distributors and healthcare facilities. The particulate matter was identified by Baxter during a stability study, and was consistent with polyethylene, the primary constituent of the film and ports used to manufacture the bag in which Nexterone is packaged.

Arthri-D Dietary Supplement: Recall – Possible Salmonella Contamination 1/24/18
Arthri-D dietary supplement Lot #1701-092, manufactured March 2017, was recalled due to potential contamination. Routine testing revealed the presence of Salmonella in one bottle from the recalled lot.

"Zero For Him" Dietary Supplement: Recall – Possible Salmonella Contamination 1/24/18
Break Ventures/California Basics recalled "Zero for Him" dietary supplement Lot #1710-638, Expiration November 2020, due to potential contamination. Routine testing revealed the presence of Salmonella in one bottle from the recalled lot. The product was distributed nationwide through Amazon.

Limbrel from Primus Pharmaceuticals, Inc.: Recall - Rare but Serious and Reversible Adverse Events 1/26/18
During 2017 there were 30 adverse event reports of elevated liver function tests or acute hypersensitivity pneumonitis associated with Limbrel products marketed as medical foods. All cases reportedly resolved without residual effects after discontinuing the product. There are four Limbrel doses/formulations affected and all lots within expiry are included in this recall. Primus voluntarily ceased its promotion and distribution of Limbrel on December 21, 2017.

Dietary Supplement Recalls & Public Notifications

In January, the FDA issued no notifications regarding undeclared active ingredients in dietary supplements to the public.

New Product Shortages Reported by the FDA:	***Date Posted***
Penicillamine tablets	1/4/18
Betaine Hydrochloride (Cystadane) for Oral Solution	1/9/18
Sodium glycerophosphate (Glycophos) injection	1/9/18
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension	1/22/18
Methylphenidate Hydrochloride (QUILLICHEW ER) Extended-Release Chewable Tablets	1/22/18
Sterile Water	1/22/18
Dorzolamide Hydrochloride Ophthalmic Solution	1/24/18
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution	1/24/18
Etoposide Injection	1/24/18

Product Discontinuations/Withdrawals:	***Date Posted***
Montelukast sodium tablets (Sandoz): 10 mg tablets. Equivalents are available.	1/3/18
Estropipate Tablets (Teva Pharmaceuticals): 0.75 mg tablets, 1.5 mg tablets, 3 mg tablets. Equivalents are available.	1/5/18
Nabumetone Tablets (Sandoz): 500 mg, 750 mg. Equivalents are available.	1/5/18
Amlodipine Besylate Tablets (Mylan Pharmaceuticals Inc.): 2.5 mg tablets, 5 mg, 10 mg. Equivalents are available.	1/9/18
Amlodipine Besylate and Benazepril Hydrochloride Capsules (Mylan Pharmaceuticals Inc.): 2.5 mg/10 mg, 5 mg/10 mg, 5 mg/20 mg, 5 mg/40 mg, 10 mg/20 mg, 10 mg/40 mg. Equivalents are available.	1/9/18
Cefepime for Injection (Apotex Corp): 1 g and 2 g vials. Equivalents are available.	1/11/18
Dronabinol Capsules (Teva Pharmaceuticals): 2.5 mg, 5 mg, 10 mg. Equivalents are available.	1/18/18
Norethindrone Acetate and Ethinyl Estradiol and Ferrous Fumarate (LOESTRIN Fe) Tablets (Teva Pharmaceuticals): 30 x 28 blister packs discontinued; 5 x 28 blister packs are available.	1/18/18
Carboplatin Injection (Mylan Pharmaceuticals Inc.): 10 mg/mL. Equivalents are available.	1/25/18
Cisplatin Injection (Mylan Pharmaceuticals Inc.): 1 mg/mL. Equivalents are available.	1/25/18
Doxorubicin Injection (Mylan Pharmaceuticals Inc.): 2 mg/mL. Equivalents are available.	1/25/18
Gemcitabine Injection (Mylan Pharmaceuticals Inc.): 2 g. Equivalents are available.	1/25/18
Ifosfamide Injection (Mylan Pharmaceuticals Inc.): 50 mg/mL. Equivalents are available.	1/25/18
Methotrexate Injection (Mylan Pharmaceuticals Inc.): 25 mg/mL. Equivalents are available.	1/25/18
Flunisolide (Aerospan) Inhalation Aerosol (Mylan Pharmaceuticals Inc.). Patients should be converted to flunisolide inhalation aerosol (Aerospan HFA, Mylan) or an alternative inhaled corticosteroid.	1/26/18

New Drug Approvals:	***Description***	***Date Approved***
Lutetium Lu 177 dotatate / Lutathera / Advanced Accelerator Applications USA Inc.	A radiolabeled somatostatin analog indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults. See attached drug summary.	1/26/18

New Indications:	***Description***	***Date Approved***
Fluarix Quadrivalent / Influenza virus vaccine / GlaxoSmithKline Biologicals	Age range expanded to include children 6 to 35 months of age	1/11/18
Olaparib / Lynparza / AstraZeneca	Treatment of metastatic breast cancer with the BRCA gene mutation	1/12/18
Afatinib / Gilotrif / Boehringer Ingelheim	First-line treatment of metastatic non-small cell lung cancer with nonresistant EGFR mutations	1/12/18
Trulance / Plecanatide / Synergy	Irritable bowel syndrome with constipation	1/24/18

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Levonorgestrel; ethinyl estradiol; ferrous bisglycinate / Balcoltra / Neuvosyn Laboratories LLC	A progestin/estrogen combination oral contraceptive	1/9/18
Metoprolol Succinate Extended-Release Capsule / Spil	Metoprolol extended release in capsule form (25 mg, 50 mg, 100 mg, 200 mg).	1/26/18
Vancomycin / Firvanq / Cutis Pharma	Vancomycin powder for oral solution, with grape-flavored diluent, for the treatment of *Clostridium difficile*-associated diarrhea and *Staphylococcus aureus* enterocolitis	1/26/18

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Lutetium Lu 177 dotatate / Lutathera / Advanced Accelerator Applications USA Inc.	
Generic Name / Brand Name / Company	Lutetium Lu 177 dotatate / Lutathera / Advanced Accelerator Applications USA Inc.
Date of approval	1/26/18
Drug Class (Mechanism of Action if novel agent)	Radiopharmaceutical; radiolabeled somatostatin analog
Indication	Treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Injection: 370 MBq/mL (10 mCi/mL) in single-dose vial. Administer 7.4 GBq (200 mCi) IV every 8 weeks for a total of 4 doses
DEA Schedule	NA
Date of market availability	Unknown
Similar Medication Names	Lutera
Clinical Use Evaluation	
Common Adverse Effects	Lymphopenia, increased GGT, vomiting, nausea, increased AST, increased ALT, hyperglycemia and hypokalemia
Severe Adverse Effects	Myelosuppression, secondary myelodysplastic syndrome and leukemia, renal toxicity, hepatotoxicity, neuroendocrine hormonal crisis, nausea and vomiting
Severe Drug-Drug Interactions	Somatostatin analogs
Severe Drug-Food Interactions	No known interactions
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Blood cell counts, serum creatinine, transaminases, bilirubin, albumin
Used in Pediatric Areas	Safety and effectiveness has not been established in pediatric patients
Renal or Hepatic Dosing	No dose adjustment is necessary in mild to moderate renal or hepatic impairment. Monitor closely in severe renal impairment. Safety has not been established in patients with severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Risk from radiation exposure, myelosuppression, secondary myelodysplastic syndrome and leukemia, renal toxicity, hepatotoxicity, neuroendocrine hormonal crisis, embryo-fetal toxicity, risk of infertility
Special administration technique or considerations	Handle with appropriate safety measures, including waterproof gloves and radiation shielding, to minimize radiation exposure. Premedicate with antiemetics 30 minutes before the recommended amino acid solution. Initiate recommended intravenous amino acid solution (containing-L-lysine and L-arginine) 30 minutes before lutetium Lu 177 dotatate infusion and continue amino acid infusion for at least 3 hours after completing lutetium infusion. Administer lutetium infusion over 30 to 40 minutes. Administer long-acting octreotide 30 mg intramuscularly 4 to 24 hours after each dose. Do not administer long-acting octreotide within 4 week of a subsequent lutetium dose; short-acting octreotide may be given for symptomatic management, but must be withheld for at least 24 hours before each lutetium dose.
Prepared by	Daniel Rutter, PharmD Student
Source	Lutathera (lutetium Lu 177 dotatate) injection [Prescribing information]. New Jersey: Advanced Accelerator Applications USA, Inc; January 2018.