Highlights of FDA Activities – 11/1/2016 – 11/30/2016

FDA Drug Safety Communications & Drug Information Updates:

Label Changes for Essure Permanent Birth Control System by Bayer Healthcare 11/15/16

Essure labeling now includes a boxed warning and a Patient Decision Checklist with the intention to support patient counseling and understanding of benefits and risks associated with Essure, as well as what to expect during and after the procedure. The boxed warning includes safety statements to clearly communicate side effects or adverse outcomes associated with this device and information about the potential need for removal.

Major Product Recalls Announced Through MedWatch:

Cantrell Drug Company Sterile Drug Products: Recall – Lack of Sterility Assurance 11/21/16

Cantrell Drug Company recalled certain unexpired sterile drug products due to lack of sterility assurance. The extensive list of recalled products distributed nationwide from 5/25/16 to 10/31/16 can be found at: http://www.fda.gov/Safety/Recalls/ucm529776.htm

Tri-Coast Pharmacy Sterile Products: Recall – Lack of Sterility Assurance 11/21/16

Tri- Coast Pharmacy Inc. recalled all sterile products prepared between 5/17/16 and 11/17/16 due to FDA concerns over the lack of sterility assurance of the drugs named in this recall. The following link contains the extensive list of the recalled drugs: http://www.fda.gov/Safety/Recalls/ucm530154.htm

Homeopathic Pediatric Products by Raritan Pharmaceuticals: Recall- Possible Belladonna Alkaloids 11/25/16

Raritan Pharmaceutical, a contract manufacturer for Homeolab USA, recalled homeopathic products containing belladonna extract due to the potential variation in the content of belladonna extract in the products compared to what was declared on the label. The recalled products, CVS Homeopathic Infants' Teething Tablet, Kids Relief Homeopathic Ear Relief Oral Liquid, and Kids Relief Homeopathic Ear Relief Oral Liquid, were distributed nationwide. The following link contains the list of specific products that were recalled: http://www.fda.gov/Safety/Recalls/ucm530618.htm

Dietary Supplement Recalls & Public Notifications

In November, 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)***
ABX Weight Loss	Weight loss	Sibutramine[1]
Megajex Natural Male Sex Enhancer*	Sexual enhancement	Sildenafil[2] and tadalafil[3]
NutriVitaShop DMAA 500 g	Stimulant, pre-workout, and weight loss	DMAA[4]
Ready Man!	Sexual enhancement	Sildenafil[2]
Side Head Regulator TT*	Headaches, migraines	Lead (elevated levels)
Skinny Bee Diet*	Weight loss	Sibutramine[1], desmethylsibutramine[5], phenolphthalein[6]

Product	***Promoted Use***	***Hidden/Undeclared Drug Ingredient(s)***
Supreme Slim 5.7	Weight loss	Sildenafil[2], phenolphthalein[6],
Ultimate Body Tox	Weight loss	Sibutramine[1]
Ultimate Body Tox PRO*	Weight loss	Sibutramine[1]

*Recalled

[1] Controlled substance that was removed from market in October 2010 for safety reason (substantial increase in blood pressure and heart rate)

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

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

[4] DMAA (1,3-dimethylamylamine, methylhexanamine, or geranium) can narrow blood vessels, causing a rise in blood pressure or other cardiovascular problems.

[5] Pharmacologically active metabolite of sibutramine

[6] Studies have indicated that this chemical may be associated with an increased risk of cancer. It is not FDA approved for inclusion in any drug product in the United States

New Product Shortages Reported by the FDA:

No new shortages announced in November 2016

Product Discontinuations/Withdrawals	***Date Posted***
Vitekta®(elvitegravir) tablets from Giliad Sciences, Inc Permanently discontinuing both the 85 mg (NDC 61958-1301-01) and 150 mg (NDC 61958-1302-1) tablets; elvitegravir remains available only in combination formulations.	10/20/16; 11/23/16
Cyclophosphamide Tablets from West-Ward Pharmaceuticals Discontinuing the 25 mg (NDC 0054-8089-25) and 50 mg (NDC 0054-4130-25, NDC0054-8130-25 NDC 0054-4130-29) tablets; 25 mg and 50 mg capsules remain available..	11/1/16
Lindane Lotion, USP 1% from Akorn Pharmaceuticals Discontinuing the lotion, NDC 61748-0401-02. Currently, no alternatives are available.	11/10/16
Lindane Shampoo, USP 1% from Akorn Pharmaceuticals Discontinuing the shampoo, NDC 61748-0400-02. Lindane 1% shampoo remains available from Morton Grove Pharmaceuticals (NDC 60432-0834-60).	11/10/16
Zofran (ondansetron) Oral Solution from Novartis Discontinuing the 4 mg/5 mL bottle of 50 mL (NDC 0173-0489-00). The oral solutions remains available from generic manufacturers.	11/17/16
Irbesartan and Hydrochlorothiazide Tablets from Mylan Discontinuing manufacture of both the 150 mg/12.5 mg (NDC 0378-3033-93) and 300 mg/12.5 mg (NDC 0378-3034-93) tablets. The product remains available from multiple other manufacturers.	11/18/16
Ocufen (Flurbiprofen sodium 0.03% ophthalmic solution, USP) from Allergan Product remains available from generic manufacturers.	11/23/16
Vibativ (telavancin) injection from Theravance Biopharma US Inc. Discontinuing the 250 mg vial (NCD 62847-002-01), the 750 mg vial continues to be available.	11/23/16
Dextrose 70% Injection, USP in 1,000 mL glass bottle from B. Braun Medical Inc. Discontinuing only the glass bottles (NDC 0262-1290-55); will continue to supply 70% dextrose 2,000 mL in plastic bags (NDC 0264-7387-50).	11/28/16
Ampicillin Capsules 250 mg, 500 mg from Par Pharmaceutical Discontinuing manufacture of ampicillin capsules 250 mg (100 and 500 count) and 500 mg (100 and 500 count) with inventory to be exhausted in 2017. NDCs 67253-180-10, 67253-180-50, 67253-181-10, 67253-181-50. This product will remain available by other manufacturers.	11/30/16

New Drug Approvals:	***Description***	***Date Approved***
Prasterone / Intrarosa / Endoceutics Inc	See attached drug summary	11/16/16
Insulin glargine, lixisenatide/ Soliqua / Anofi Aventis US	See attached drug summary	11/21/16
Insulin degludec, liraglutide/ Xultophy / Novo Nordisk Inc.	See attached drug summary	11/21/16

New Indications:	***Description***	***Date Approved***
Etanercept / Enbrel / Amgen	Moderate to severe plaque psoriasis in children 4 to 17 years of age	11/4/16
Nivolumab / Opdivo / Bristol-Myers Squibb Company	Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after platinum-based therapy	11/10/16
Daratumumab / DARZALEX / Janssen Biotech, Inc.	Multiple myeloma in patients who have received prior therapy. Daratumumab is to be used in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone.	11/21/16

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Maraviroc / Selzentry / ViiV Healthcare	Oral solution 20 mg/mL and lower strength tablets (25 mg and 75 mg) for use in patients 2 years of age and older weighing at least 10 kg	11/4/16
Doxylamine succinate and pyridoxine HCl extended-release tablet / Bonjesta / Duchesnay	New extended release dosage form for once or twice daily administration	11/7/16
Tenofovir alafenamide / Vemlidy / Gilead	New single ingredient tenofovir alafenamide 25 mg tablet for the treatment of hepatitis B infection	11/10/16

Compiled by:

Terri Levien, Pharm.D.
Zaynah Ali, Pharm.D., PGY1 Drug Information Resident
Luke Dearden, Pharm.D., PGY1 Providence Ambulatory Care Resident
Melissa Apperson, Pharm.D. Candidate 2017
Patricia Snel, U.W. Pharm.D. Candidate 2017
Alice Knotts, Pharm.D. Candidate 2018
Uzoma Mbogu, Pharm.D. Candidate 2018

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

Prasterone / Intrarosa / Endoceutics	
Generic Name / Brand Name / Company	Prasterone / Intrarosa / Endoceutics Inc
Date of approval	11/16/16
Drug Class (Mechanism of Action if novel agent)	Inactive endogenous steroid that is converted into active androgens and/or estrogens. The mechanism of action in postmenopausal women with vulvar and vaginal atrophy is not fully established.
Indication	Treatment of moderate-to-severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause

Comparative agent – Therapeutic interchange?	Ospemifene, vaginal estrogens
Dosage forms/strengths. Common Dose/sig	Vaginal insert: 6.5 mg of prasterone One vaginal insert, once daily at bedtime
DEA Schedule	Not scheduled
Date of market availability	Early 2017
Similar Medications (Look-Alike Sound-Alike)	Prostacyclin, Prostaglandin, Paroxetine, Piracetam
Clinical Use Evaluation	
Common Adverse Effects	Vaginal discharge; abnormal pap smear
Severe Adverse Effects	None known
Severe Drug-Drug Interactions	None known
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?)	Pap smear
Used in Pediatric Areas	Safety and effectiveness have not been established in pediatric patients
Renal or Hepatic Dosing	The effect of renal or hepatic impairment on the pharmacokinetics has not been studied
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Undiagnosed abnormal genital bleeding: Any postmenopausal woman with undiagnosed persistent or recurring genital bleeding should be evaluated to determine the cause of the bleeding before consideration of treatment
Special administration technique or considerations	Supplied with single-use applicators. Patients should be instructed to empty bladder and wash hands before handling the vaginal insert and applicator.
Prepared by	Melissa K. Apperson PharmD Candidate 2017
Source	Intrarosa (prasterone) vaginal insert [prescribing information]. Quebec City, Canada: Endoceutics Inc; November 2016.

Insulin glargine, lixisenatide / Soliqua 100/33 / Sanofi-Aventis US	
Generic Name / Brand Name / Company	Insulin glargine and lixisenatide injection/Soliqua 100/33 / Sanofi-Aventis
Date of approval	11/21/16
Drug Class (Mechanism of Action if novel agent)	A combination of insulin glargine, a long-acting insulin, and lixisenatide, a glucagon-like peptide 1 (GLP-1) receptor agonist.
Indication	As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes, who are uncontrolled on basal insulin (less than 60 units daily) or lixisenatide.
Comparative agent – Therapeutic interchange?	Insulin degludec and liraglutide injection (Xultophy)
Dosage forms/strengths. Common Dose/sig	Prefilled, disposable, single-patient use 3 mL pen: 100 units of insulin glargine and 33 mcg lixisenatide per mL. Inject once a day within an hour before the first meal of the day. Starting dose is 15 units insulin glargine/5 mcg lixisenatide for patients inadequately controlled on less than 30 units of basal insulin or on lixisenatide alone. Starting dose is 30 units insulin glargine/10 mcg lixisenatide for patients inadequately controlled on 30 to 60 units of basal insulin.
DEA Schedule	Not scheduled
Date of market availability	January 2017
Similar Medications (Look-Alike Sound-Alike)	Solage Topical Solution, Solia, Soliris

Clinical Use Evaluation	
Common Adverse Effects	Hypoglycemia, allergic reactions, nausea, nasopharyngitis, diarrhea, upper respiratory tract infection, & headache
Severe Adverse Effects	Hypoglycemia, anaphylaxis and hypersensitivity
Severe Drug-Drug Interactions	Lixisenatide delays gastric emptying and may reduce how fast medications are absorbed. Use caution when giving with medications that have a narrow therapeutic window or require clinical monitoring. Use caution in patients on other antidiabetic agents; closely monitor blood glucose
Severe Drug-Food Interactions	Administer within the hour prior to the first daily meal.
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Monitor blood glucose levels and hemoglobin A1C
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	Patients with severe renal impairment (eGFR <30 to 15 mL/min/1.73m^2) should be monitored closely for gastrointestinal adverse reactions and for changes in renal function. Use is not recommended in patients with end-stage renal disease. The effect of hepatic impairment has not been studied.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Not to be used during a hypoglycemic event or in patients who have a hypersensitivity to the product, insulin glargine, lixisenatide, or any of the product excipients. Consider all the cautions associated with insulin glargine and lixisenatide.
Special administration technique or considerations	Discontinue therapy with insulin glargine or lixisenatide prior to initiating therapy with the combination. Can be injected in the upper arms, stomach or thigh, and injection sites should be rotated. A new sterile needle should be used with each administration and the injection site should be cleaned with an alcohol swab. Safety check (conducted by turning dose selector to the 2 mark and pressing injection button) must be conducted before each injection. Store in refrigerator until first use, then store at room temperature and use for up to 14 days.
Prepared by	Melissa Apperson PharmD Candidate 2017
Source	Soliqua 100/33 (insulin glargine and lixisenatide injection) [prescribing information]. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; November 2016.

Insulin degludec and liraglutide / Xultophy 100/3.6 / Novo Nordisk	
Generic Name / Brand Name / Company	Insulin degludec and liraglutide injection/ Xultophy/ Novo Nordisk Inc.
Date of approval	11/21/16
Drug Class (Mechanism of Action if novel agent)	A combination of insulin degludec, a long-acting insulin, and liraglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist.
Indication	Indicated for the improvement of glycemic control in adults with type 2 diabetes mellitus inadequately controlled on basal insulin (less than 50 units daily) or liraglutide (less than or equal to 1.8 mg/day).
Comparative agent – Therapeutic interchange?	Insulin glargine / liraglutide (Soliqua 100/33)
Dosage forms/strengths. Common Dose/sig	Injection: 100 units of insulin degludec per mL and 3.6 mg of liraglutide per mL in a 3 mL single-patient-use pen. Starting dose 16 units insulin degludec/0.58 mg liraglutide; maximum dose 50 units insulin degludec/1.8 m liraglutide
DEA Schedule	Not scheduled
Date of market availability	First half of 2017

Similar Medications (Look-Alike Sound-Alike)	Xulane
Clinical Use Evaluation	
Common Adverse Effects	Nasopharyngitis, headache, nausea, diarrhea, increased lipase and upper respiratory tract infection
Severe Adverse Effects	Risk of thyroid c-cell tumors, pancreatitis, hypoglycemia, acute kidney injury, hypersensitivity, hypokalemia
Severe Drug-Drug Interactions	Liraglutide delays gastric emptying and may reduce how fast medications are absorbed. Use caution when giving with medications that have a narrow therapeutic window or require clinical monitoring. Use caution in patients on other antidiabetic agents; closely monitor blood glucose
Severe Drug-Food Interactions	None
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Monitor blood glucose and hemoglobin A1c levels.
Used in Pediatric Areas	Safety and efficacy has not been established in pediatric patients.
Renal or Hepatic Dosing	Limited data in mild-moderate renally impaired patients taking the combination. Additional glucose monitoring and dose adjustments may be required on an individual basis. Has not been studied in severe renal impairment. The combination has not been studied in patients with hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications • Patients with a personal or family history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome type 2 • Patients with prior serious hypersensitivity reaction to the product or either of the active substances or any of its excipients • During episode of hypoglycemia Consider all the cautions associated with insulin degludec and liraglutide
Special administration technique or considerations	• Discontinue therapy with liraglutide or basal insulin prior to initiation of the combination. • Administer once daily at same time each day with or without food. • Maximum daily dosage is 50 units (50 units of insulin degludec and 1.8 mg of liraglutide). • Use alternative antidiabetic products if patients require daily dosages persistently below 16 units or over 50 units. • Inject subcutaneously in thigh, upper arm or abdomen. • A new sterile needle should be used with each administration and the injection site should be cleaned with an alcohol swab • Priming (conducted by turning dose selector to priming mark and pressing injection button) must be conducted before each injection. • Store in refrigerator until first use, then store at room temperature or in the refrigerator, and use for up to 21 days.
Prepared by	Uzoma Mbogu, Pharm.D. Candidate of 2018
Source	Xultophy 100/3.6 (Insulin degludec and liraglutide) injection [prescription information]. Plainsboro, NJ: Novo Nordisk Inc.; November 2016.