Highlights of FDA Activities – 2/1/17 – 2/28/17

FDA Drug Safety Communications & Drug Information Updates:

Chlorhexidine Gluconate: Drug Safety Communication - Rare But Serious Allergic Reactions 2/2/17
The FDA is warning that skin antiseptic products containing chlorhexidine gluconate may cause serious allergic reactions. Although the allergic reactions are rare, the number of reported cases have increased. Manufacturers of the antiseptic products will now be required to add a warning to their Drug Facts label.

Major Product Recalls Announced Through MedWatch:

Ibuprofen Lysine Injection, 20 mg/2 mL by Exela Pharma Sciences: Recall - Particulate Matter 2/9/17
Exela Pharma Sciences and X-Gen Pharmaceuticals recalled ibuprofen lysine injection vials (lot # PLND1613) to the user level due to the presence of particulate matter in some of the vials.

Alaris Syringe Pump Module (Large Volume Pump), Model 8100 and AIL Sensor Kits by CareFusion: Recall - Alarm Error 2/9/17
Carefusion recalled the Alaris Syringe Pump (product numbers 147083-102 and 49000221) due to a faulty Air-In-Line (AIL) sensor that may cause a false alarm, thereby interrupting the infusion pump from delivering fluids.

HCG (Human Chorionic Gonadotropin) Freeze Dried Vials by Synergy Rx: Recall - Lack of Sterility Assurance 2/16/17
Synergy Rx Pharmacy recalled all lots of HCG 5,000 units/vial and 11,000 units/vial to the retail level due to lack of sterility assurance. The products were distributed between 6/1/2016 and 12/22/2016 to physician and clinics in California, Minnesota, Wisconsin, and Arizona.

Avella Specialty Pharmacy Sterile Products Labeled "Latex Free": Recall – May Contain Latex 2/24/17
Advanced Pharma recalled all unexpired sterile injectable products labeled "latex free" that were produced at Advanced Pharma, Inc's Houston location between September 1, 2016 and February 16, 2017 to the user level because the products may contain synthetic latex and/or natural latex. Affected product from the Houston location may have been sent to AL, AZ, CA, CO, CT, DE, FL, GA, MS, NC, NJ, OH, OK, OR, PA, SC, TN, TX, UT and VA.

Alprostadil for Injection (Edex), 10 mcg (2 pack) by Endo Pharmaceuticals: Recall - Potential Lack of Sterility 2/27/17
Endo Pharmaceuticals Inc. recalled one lot of Edex (alprostadil for injection) 10 mcg to the consumer level following detection by Endo of a defect in the crimp caps used in the manufacture of the subject product lot. This defect could impact the product's sterility assurance. The recall applies to the 10 mcg strength, packaged in a 2 pack carton (NDC 52244-010-02), product lot number 207386, Expiration Date: May 2019. The affected lot was distributed from 12/13/2016 through 2/13/2017.

Dietary Supplement Recalls & Public Notifications

In February, 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)***
Ginseng for Reinforcing Kidney	Sexual enhancement	Sildenafil[1]
Goldreallas Original	Sexual enhancement	Sildenafil[1]
Goldreallas XXX	Sexual enhancement	Sildenafil[1]
Lean Extreme Max	Weight loss	Sibutramine[2]
Old Chinese	Sexual enhancement	Sildenafil[1]
Platinum Max Strength Blue Pill	Weight loss	Sibutramine[2]
Platinum Weight Loss Solution – Fat Loss Metabolizer	Weight loss	Sibutramine[2]
Shenjingpian	Sexual enhancement	Sildenafil[1]
Slimming Plus Advanced	Weight loss	Sibutramine[2]
Well Balance Xanthium & Siler Combo (Bi Yan Pian)	Dietary supplement	Ephedra alkaloids (ma huang)
XtraHRD Natural Male Enhancement*	Sexual enhancement	Tadalafil[1]
X-treme Beauty Slim	Weight loss	Sibutramine[2]

*Recalled

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

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

New Product Shortages Reported by the FDA:	***Date Initially Posted***
Sterile Talc Powder (Lymol Medical Corp) NDC 6256-200-05	2/16/17
Sclerosol Intrapleural Aerosol (Lymol Medical Corp) NDC 6256-100-30	2/16/17

Product Discontinuations/Withdrawals	***Date Posted***
Colistimethate Sodium Injection (Perrigo Pharmaceuticals): Perrigo Pharmaceuticals discontinued manufacturing NDC 00574-0858-01; colistimethate sodium injection remains available from other manufacturers.	2/7/17
Amlodipine Besylate and Benazepril Hydrochloride Capsules (Novartis): Novartis discontinued manufacturing the following tablets: 2.5 mg/10 mg (NDC 0781-2271-01), 5 mg/10 mg (NDC 0781-2272-01), 5 mg/20 mg (NDC 0781-2273-01), 5 mg/40 mg (NDC 0781-2277-01), 10 mg/20 mg (NDC 0781-2274-01), and 10 mg/40 mg (NDC 0781-2279-01); the brand Lotrel will continue to be manufactured and there are approved generics for this product.	2/8/17

New Drug Approvals:	***Description***	***Date Approved***
Etelcalcetide / Parsabiv / Kai Pharms	See attached drug summary	2/7/17
Deflazacort / Emflaza / Marathon Pharmaceuticals, LLC	See attached drug summary	2/9/17
Brodalumab / Siliq / Valeant Pharmaceuticals	See attached drug summary	2/15/17
Telotristat ethyl / Xermelo / Lexicon Pharmaceuticals	See attached drug summary	2/27/17

New Indications:	***Description***	***Date Approved***
Opdivo / Nivolumab / Bristol-Myers Squibb	Treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with a platinum-containing chemotherapy.	2/2/17
Revlimid / Lenalidomide / Celgene	Maintenance treatment therapy for patients with multiple myeloma following autologous stem cell transplant.	2/22/17
Ombitasvir, paritaprevir, and ritonavir / Technivie / Abbvie	Indication expanded to include patients with genotype 4 chronic hepatitis C virus infection with compensated cirrhosis	2/14/17

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Dapagliflozin; saxagliptin / Qtern / AstraZeneca	New combination tablet dosage form	2/27/17

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Etelcalcetide / Parsabiv / Amgen	
Generic Name / Brand Name / Company	Etelcalcetide / Parsabiv / Amgen
Date of approval	February 7, 2017
Drug Class (Mechanism of Action if novel agent)	Calcium-sensing receptor (CaSR) agonist; calcimimetic, acts to decrease parathyroid hormone (PTH) secretion
Indication	Secondary hyperparathyroidism in adult patients with chronic kidney disease on hemodialysis.
Comparative agent – Therapeutic interchange?	Cinacalcet
Dosage forms/strengths. Common Dose/sig	Injection: 2.5 mg/0.5 mL, 5 mg/mL, 10 mg/2 mL. Starting dose: 5 mg as an IV bolus injection three times per week at the end of hemodialysis. Usual dosage range is 2.5 to 15 mg three times per week titrated based on PTH and corrected serum calcium response.
DEA Schedule	Not applicable
Date of market availability	Not known
Similar Medications (Look-Alike Sound-Alike)	Calcifediol
CLINICAL USE EVALUATION	
Common Adverse Effects	≥ 5%: blood calcium decreased, muscle spasms, diarrhea, nausea, vomiting, headache, hypocalcemia, paresthesia
Severe Adverse Effects	Hypocalcemia, heart failure, upper GI bleeding
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?)	Measure serum calcium within 1 week after initiation or dose adjustment, and then every 4 weeks. Measure PTH 4 weeks after initiation or dose adjustment.
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	Only for use in patients with chronic kidney disease on hemodialysis; not recommended for use in patients not receiving hemodialysis.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in patients with known hypersensitivity to etelcalcetide or any of the product ingredients. Cautions: Hypocalcemia: monitor serum calcium levels closely; discontinue if corrected serum calcium falls below 7.5 mg/dL or with symptoms of hypocalcemia. Worsening heart failure: reduction in corrected serum calcium may correlate with worsening congestive heart failure. Upper GI bleeding: closely monitor patients with risk factors for GI bleeding.
Special administration technique or considerations	Administer only at the end of hemodialysis. Administer by IV bolus injection into the venous line of the dialysis circuit at the end of the hemodialysis treatment during rinse back or administer IV after rinse back. Do not mix or dilute prior to administration.
Prepared by	Terri L. Levien, Pharm.D.
Source	Parsabiv (etelcalcetide) injection prescribing information. Thousand Oaks, CA: Amgen; February 2017.

Deflazacort / Emflaza / Marathon Pharmaceuticals, LLC	
Generic Name / Brand Name / Company	Deflazacort / Emflaza / Marathon Pharmaceuticals, LLC
Date of approval	February 9, 2017
Drug Class (Mechanism of Action if novel agent)	Corticosteroid
Indication	Treatment of Duchenne muscular dystrophy in patients 5 years of age and older
Comparative agent – Therapeutic interchange?	Prednisone
Dosage forms/strengths. Common Dose/sig	Tablets: 6 mg, 18 mg, 30 mg, 36 mg; Oral suspension: 22.75 mg/ml; Once daily dosed at 0.9 mg/kg/day
DEA Schedule	Not scheduled
Date of market availability	1st Quarter 2017
Similar Medications (Look-Alike Sound-Alike)	None identified
CLINICAL USE EVALUATION	
Common Adverse Effects	>10%: Cushingoid appearance, weight increased, increased appetite, upper respiratory tract infection, cough, pollakiuria, hirsutism, central obesity, and nasopharyngitis; >5%: erythema, irritability, rhinorrhea, abdominal discomfort
Severe Adverse Effects	Increased risk of infections; gastrointestinal perforation; skin rashes; anaphylaxis
Severe Drug-Drug Interactions	Avoid use with moderate to strong CYP3A4 inhibitors or inducers (dose adjustments recommended if unavoidable) and neuromuscular blockers
Severe Drug-Food Interactions	Do not administer with grapefruit juice
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Long term use may require monitoring of sodium and potassium levels, bone mineral density, and intraocular pressure
Used in Pediatric Areas	Not approved for use in children less than 5 years of age
Renal or Hepatic Dosing	No renal adjustments; No hepatic adjustments for mild to moderate impairment but no clinical experience/recommendation provided for severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	**Contraindicated** in patients with hypersensitivity to deflazacort or any of the inactive ingredients Discontinuation must be done gradually if drug has been administered for more than a few days Chronic use can cause alterations in endocrine function (HPA axis suppression, Cushing's syndrome, hyperglycemia), decreased bone density, ophthalmic effects (cataracts, infections, glaucoma, change of intraocular pressure; > 6 week use); negative growth/development effects on children Immunosuppression may occur with masked signs and symptoms; do not administer live or live attenuated vaccines to patients receiving immunosuppressive doses Alteration in cardiovascular/renal function can occur (elevated blood pressure, salt/water retention, increased potassium/calcium excretion) Behavioral and mood disturbances may occur (euphoria, insomnia, mood swings, personality changes, severe depression and psychosis) Serious skin rashes may occur Increased risk of gastrointestinal perforation Increased risk of thromboembolic events with higher cumulative doses
Special administration technique or considerations	Taken with or without food, tablets can be crushed and mixed with applesauce, mix suspension well prior to administration; use only the oral dispenser provided with the oral suspension.
Prepared by	Andrew Pascal, Pharm.D. student, class of 2017
Source	Emflaza (deflazacort) tablets prescribing information. Northbrook, IL: Marathon Pharmaceuticals; February 2017.

Brodalumab/ Siliq / Valeant Pharmaceuticals	
Generic Name / Brand Name / Company	Brodalumab/ Siliq / Valeant Pharmaceuticals
Date of approval	February 15, 2017
Drug Class (Mechanism of Action if novel agent)	IgG2k antibody antagonist directed against human interleukin-17 receptor
Indication	Treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies
Comparative agent – Therapeutic interchange?	Ixekizumab, secukinumab
Dosage forms/strengths. Common Dose/sig	Injection: 210 mg/1.5 mL prefilled syringe; 210 mg subcutaneous injection on weeks 0, 1, 2 followed by 210 mg every 2 weeks
DEA Schedule	Not scheduled
Date of market availability	Expected 2nd half 2017
Similar Medications (Look-Alike Sound-Alike)	Silace, Sildeq
CLINICAL USE EVALUATION	
Common Adverse Effects	>1%: arthralgia, headache, fatigue, diarrhea, oropharyngeal pain, nausea, myalgia, injection site reactions, influenza, neutropenia and tinea infections.
Severe Adverse Effects	Development of Crohn's disease, latent tuberculosis reactivation, increased risk of infections and recurrent infections, suicidal thoughts and behaviors, neutropenia
Severe Drug-Drug Interactions	Avoid use of live vaccines in patients treated with brodalumab; May alter CYP450 enzyme levels, consider dose adjustments of concurrent CYP450 substrate medications upon initiation and discontinuation of brodalumab
Severe Drug-Food Interactions	N/A
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Evaluate patient for tuberculosis infection prior to initiating therapy
Used in Pediatric Areas	Not evaluated in pediatric patients
Renal or Hepatic Dosing	No renal or hepatic dose recommendations
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	**Contraindicated** in patients with Crohn's disease; discontinue in patients who develop Crohn's disease while taking brodalumab **Black box warning** of suicidal ideation/behavior including completed suicides that occurred in patients treated with brodalumab; cases of worsening thoughts or behaviors should be referred to a mental health professional, available only through REMS program due to suicidal risks Increased risk of infections may occur as well as recurrent infections; Due to risks of reactivation of latent tuberculosis (TB), consider anti-TB treatment in patients with past history of latent or active TB and monitor for signs of active infection after brodalumab initiation Worsening/exacerbation of Crohn's disease may occur, do not use in patients with diagnosed Crohn's disease and discontinue use in patients who develop Crohn's disease while taking brodalumab Avoid live vaccine use while on brodalumab due to increased risk of infections As with all other therapeutic proteins, there is risk of patient immunogenicity and antibody formation against brodalumab may decrease efficacy
Special administration technique or considerations	Administered as a subcutaneous injection; Injection sites are subcutaneous tissues around the abdomen, thigh, and outer arm area; Pinching subcutaneous tissues creates firm surface for injection; Do not inject into areas where the skin is tender, bruised, red, hard, thick, scaly, or affected by psoriasis; Insert needle between 45 and 90 degrees into the skin for injection

Prepared by	Andrew Pascal, Pharm. D. student, class of 2017
Source	Siliq (brodalumab) injection prescribing information. Bridgewater, NJ: Valeant Pharmaceuticals; February 2017.

Telotristat ethyl / Xermelo / Lexicon Pharmaceuticals	
Generic Name / Brand Name / Company	Telotristat ethyl / Xermelo / Lexicon Pharmaceuticals
Date of approval	February 27, 2017
Drug Class (Mechanism of Action if novel agent)	Tryptophan hydroxylase inhibitor; reduces the production of peripheral serotonin which is overproduced in patients with carcinoid syndrome.
Indication	Use in conjunction with a somatostatin analog for the treatment of carcinoid syndrome diarrhea inadequately controlled with a somatostatin analog.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Tablets: 250 mg. Dose: 250 mg three times daily
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Trelstar
CLINICAL USE EVALUATION	
Common Adverse Effects	All ≥5%: nausea, headache, increased GGT, depression, flatulence, decreased appetite, peripheral edema, pyrexia
Severe Adverse Effects	Constipation
Severe Drug-Drug Interactions	CYP3A4 substrates – efficacy of CYP3A4 substrates may be reduced
Severe Drug-Food Interactions	Absorption increased with administration with food
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	None required
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	No adjustments in renal impairment; has not been studied in end-stage renal disease requiring hemodialysis. No adjustments in mild hepatic impairment; the effects of moderate or severe hepatic impairment have not been assessed.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Constipation: discontinue if severe constipation or severe persistent or worsening abdominal pain occurs.
Special administration technique or considerations	Administer with food. When used with short-acting octreotide, administer octreotide at least 30 minutes after administering telotristat.
Prepared by	Terri L. Levien, Pharm.D.
Source	Xermelo (telotristat ethyl) tablet prescribing information. The Woodlands, TX: Lexicon Pharmaceuticals, Inc.; February 2017.