Highlights of FDA Activities – 12/1/15 – 12/31/15

FDA Drug Safety Communications & Drug Information Updates:

FDA Drug Safety Communication: FDA Revises Labels of SGLT2 Inhibitors for Diabetes to Include Warnings about Ketoacidosis and Serious Urinary Tract Infections 12/4/15

A FDA safety review has prompted additions to the Warnings and Precautions sections of the labeling of all sodium-glucose cotransporter-2 (SGLT-2) inhibitors describing the risk of ketoacidosis and of serious urinary tract infections, and providing monitoring recommendations. A review of the FDA Adverse Event Reporting System (FAERS) database identified 73 cases of ketoacidosis related to the use of SGLT-2 inhibitors and 19 cases of life-threatening blood infections and kidney infections.

Baclofen Active Pharmaceutical Ingredient from Taizhou Xinyou Pharmaceutical and Chemical: FDA Statement - FDA Warns of Potential Contamination 12/9/15

The FDA alerted drug compounders that certain lots of baclofen active pharmaceutical ingredient manufactured by Taizhou Xinyou Pharmaceutical & Chemical Co., Limited from Taizhou City, Zhejiang Province, China, may be at risk for contamination with particulates and should not be used for compounding. This company manufactures ingredients for re-packagers and distributors, which in turn may be sold for distribution in the United States. The FDA has concluded via communication with Taizhou that the baclofen ingredient in question is not suitable for use in compounding sterile products, especially in cases where the compounded formulation may be injected into the spinal column. The suspected contaminants of this ingredient include particulates, endotoxin, and microorganisms. The FDA recommends against the use of any baclofen products from Taizhou.

Rosiglitazone-containing Diabetes Medicines: Drug Safety Communication - FDA Eliminates the Risk Evaluation and Mitigation Strategy (REMS) 12/16/15

The FDA has eliminated the Risk Evaluation and Mitigation Strategy (REMS) for rosiglitazone and rosiglitazone-containing medications, which include the brand name drugs Avandia, Avandamet, and Avandaryl in addition to generic formulations. This means that the FDA has deemed a REMS is no longer necessary to ensure the benefits of rosiglitazone outweigh the risks. The FDA had previously removed prescribing restrictions in 2013 when data did not demonstrate an increased risk of heart attack when compared to metformin and sulfonylureas. Additional data has not yielded additional relevant safety information upon further monitoring.

Major Product Recalls Announced Through MedWatch:

Digital Temple Thermometer (DTT) by K-Jump Health Co., Ltd.: Recall - Inaccurate Temperature Display 12/1/2015

Bestmed, LLC has recalled some of their Digital Temple Thermometers as they may display inaccurate temperatures, potentially delaying necessary care. The model that is being recalled is a hand-held model, with a sticker on the back that reads "KD-2201." In the US or Canada, the Digital Temple Thermometer could have been purchased from Bestmed, Good Neighbor, Kroger, Medline, Meijer, Premier Value, Safeway, Life Brand, Target, Top Care, Best Choice, or Western Family. If this product was purchased, Bestmed requests that they be contacted via phone at (877) 299-6700 to arrange a replacement or refund.

OmniPod Insulin Management System by Insulet: Field Safety Notification - Reported Cases of Needle Mechanism Deployment Failure or Delay 12/2/15 & 12/23/15

Insulet Corporation initiated a voluntary Field Safety Notification for 15 different lots of the OmniPod distributed in the U.S. and for 3 different lots distributed internationally. This recall is due to an increase in the reported instances of the Pod's needle mechanism failing to deploy, or there being a delay in the needles release, resulting in an interruption of insulin delivery. Customers with Pods from the affected lots have been contacted by Insulet to ensure accuracy of their device.

The Etest PIP/TAZO/CON-4 PTC 256 Recalled by bioMerieux – Potential for Test Result Error 12/29/15
Products with manufacturing dates between December 20, 2012 and October 23, 2015 distributed between January 24, 2013 and November 9, 2015 are affected. Unused tests should be discarded. Results from used Etests should be re-visited, as the product may indicate that PIP/TAZO therapy is effective when it is not.

4mg Norepinephrine Bitartrate (16 mcg/mL) in 0.9% Sodium Chloride in 250 mL Viaflex Bag and 8 mg Norepinephrine Bitartrate (32 mcg/mL) in 0.9% Sodium Chloride in 250 mL Viaflex Bag Voluntarily Recalled by PharMEDium for Discoloration 12/31/15
Due to complaints received from hospitals that some products were found to have a discoloration in the admixture, 29 lots of 4 mg Norepinephrine Bitartrate (16mcg/mL) in 0.9% Sodium Chloride in 250 mL Viaflex Bag and 3 lots of 8 mg Norepinephrine Bitartrate (32 mcg/mL) in 0.9% Sodium Chloride in 250 mL Viaflex Bag are being recalled. Affected lots are listed in the firm's press release (http://www.fda.gov/Safety/Recalls/ucm479677.htm).

Dietary Supplement Recalls & Public Notifications

In December, 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)***
Apexxx*	Sexual enhancement	Sildenafil
Diamond 3500	Sexual enhancement	Sildenafil, tadalafil
Eros Power Zone 1900	Sexual enhancement	Desmethyl carbodenafil, dapoxetine
Fuel Up Plus*	Sexual enhancement	Hydroxythiohomosildenafil
Fuel Up High Octane*	Sexual enhancement	Hydroxythiohomosildenafil
OrgaZen 3000	Sexual enhancement	Tadalafil
OragZen 3500	Sexual enhancement	Tadalafil
Power Tiger-X	Sexual enhancement	Sulfosildenafil
Rhino 7 Blue 9000	Sexual enhancement	Tadalafil
Rhino Big Horn 3000	Sexual enhancement	Tadalafil, desmethyl carbodenafil
Triple PowerZen Gold 2000	Sexual enhancement	Sildenafil, tadalafil
Triple PowerZen Plus 2000	Sexual enhancement	Sildenafil, tadalafil
Triple MiracleZen Plus 1500 mg	Sexual enhancement	Sildenafil, tadalafil, dapoxetine
Triple MiracleZen Gold 1750 mg	Sexual enhancement	Sildenafil, tadalafil, dapoxetine
Triple MiracleZen Extreme 1750 mg	Sexual enhancement	Sildenafil, tadalafil, dapoxetine
X Again Platinum	Sexual enhancement	Sildenafil, tadalafil, dapoxetine
Xtra Zone 2600	Sexual enhancement	Sildenafil, tadalafil
Xtra Zone 2400	Sexual enhancement	Sildenafil, tadalafil
Xtra Zone 2200	Sexual enhancement	Sildenafil, tadalafil
Xtra Zone 2400	Sexual enhancement	Sildenafil, tadalafil
Asset Bold*	Weight loss	Sibutramine, phenolphthalein
Asset Extreme Plus*	Weight loss	Sibutramine, phenolphthalein
Evolve or Evolve Bee Pollen*	Weight loss	Sibutramine, phenolphthalein
Infinity*	Weight loss	Sibutramine, phenolphthalein
Jenesis*	Weight loss	Sibutramine, phenolphthalein

La'Trim Plus*	Weight loss	Sibutramine, phenolphthalein
Lipo Escultura*	Weight loss	Diclofenac, sibutramine
Oasis or Oasis Bee Pollen*	Weight loss	Sibutramine, phenolphthalein
Pink Bikini (Lucy's Weight Loss System)*	Weight loss	Diclofenac
Prime or Prime Bee Pollen*	Weight loss	Sibutramine, phenolphthalein
SlimeX-15*	Weight loss	Sibutramine, phenolphthalein
Slim Trim U*	Weight loss	Sibutramine, phenolphthalein
Smart Lipo*	Weight loss	Sibutramine, desmethylsibutramine, phenolphthalein
Thirty Plus	Weight loss	Sibutramine
Ultimate Formula*	Weight loss	Sibutramine, phenolphthalein
Xcel and Xcel Advanced*	Weight loss	Sibutramine, phenolphthalein
Zi Xiu Tang*	Weight loss	Sibutramine, phenolphthalein

*Recalled

New Product Shortages Reported by the FDA:	***Date Initially Posted***
Tigecycline (Tygacil) for Injection (Pfizer Pharmaceuticals, 50 mg/10 mL vial)	12/10/15
Morphine Sulfate Injection, USP, CII (Preservative Free, for PCA use only) (Hospira, Inc., 1 mg/mL and 5 mg/mL, 30 mL vials)	12/14/15
Eptifibatide (Integrilin) Injection (Merck Sharp & Dohme Corp., 20 mg/10 mL, 75 mg/100 mL, 200 mg/100 mL)	12/18/15

Product Discontinuations/Withdrawals	***Date Posted***
Ofloxacin Otic Solution 0.3% (Sandoz) Remains available from other generic manufacturers	12/2/15
Rivastigmine Tartrate Capsules (Exelon, Novartis) Remains available from generic manufacturers	12/4/15
Castor Oil, Balsam Peru, and Trypsin topical spray (Granulex Aerosol Spray, Mylan) TBC aerosol by Delta Pharmaceutical currently remains available	12/24/15

New Drug Approvals:	***Description***	***Date Approved***
Sebelipase alfa / Kanuma / Alexion Pharmaceuticals Inc.	See attached drug summary	12/8/15
Vonicog alfa (von Willebrand Factor, recombinant) / Vonvendi / Baxalta U.S., Inc.	See attached drug summary	12/8/15
Alectinib / Alecensa / Genentech	See attached drug summary	12/11/15
Uridine triacetate / Vistogard / Wellstat Therapeutics Corporation	See attached drug summary	12/11/15
Sugammadex / Bridion / Organon USA Inc.	See attached drug summary	12/15/15
Insulin glargine / Basaglar / Eli Lilly & Co.	Same as reference listed Lantus (insulin glargine)	12/15/15
Selexipag / Uptravi / Actelion Pharmaceuticals US, Inc.	See attached drug summary	12/21/15
Lesinurad / Zurampic / AstraZeneca Pharmaceuticals LP	See attached drug summary	12/22/15

New Indications:	***Description***	***Date Approved***
Human papillomavirus 9-valent vaccine / Gardasil 9 / Merck & Co., Inc.	Indication expanded to include use in males ages 16 through 26	12/15/15
Pembrolizumab / Keytruda / Merck & Co., Inc.	Indication expanded to include use as first-line treatment for patients with unresectable or metastatic melanoma	12/18/15
IncobotulinumtoxinA injection / Xeomin / Merz North America	Adult upper limb spasticity	12/22/15

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Methylphenidate hydrochloride / QuilliChew ER / Pfizer Inc.	QuilliChew ER, the first FDA-approved chewable formulation of methylphenidate, is indicated for use in patients age 6 years or older with Attention Deficit Hyperactivity Disorder (ADHD). It will be available in 20 mg, 30 mg, and 40 mg scored tablets.	12/4/15
Bendamustine hydrochloride / Bendeka / Eagle Pharmaceuticals, Inc.	See attached drug summary; low-volume bendamustine formulation indicated for treatment of patients with chronic lymphocytic leukemia (CLL), as well as patients with indolent B-cell non-Hodgkin lymphoma that has progressed during or within 6 months of a treatment with rituximab or a regimen containing rituximab.	12/7/15
Ciprofloxacin / Otiprio / Otonomy Inc.	Otiprio is a ciprofloxacin 6% otic suspension indicated for treatment of pediatric patients with bilateral otitis media with effusion undergoing tympanostomy tube placement.	12/10/15
Aprepitant oral suspension / Emend / Merck	The powder for oral suspension formulation is approved for prevention of chemotherapy induced nausea and vomiting in patients 6 months of age and older	12/17/15

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Sebelipase alfa / Kanuma / Alexion Pharmaceuticals Inc.	
Generic Name / Brand Name / Company	Sebelipase alfa / Kanuma / Alexion Pharmaceuticals Inc.
Date of approval	12/8/15
Drug Class (Mechanism of Action if novel agent)	Recombinant human lysosomal acid lipase (rhLAL) that catalyzes the lysosomal hydrolysis of cholesteryl esters and triglycerides, creating free cholesterol, glycerol, and free fatty acids
Indication	Treatment of patients diagnosed with Lysosomal Acid Lipase (LAL) deficiency, a rare condition where the body does not produce enough LAL, affecting fat metabolism
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Injection: 20 mg/10 mL (2 mg/mL) solution in single-use vials; for continuous IV infusion, with recommended weight-based dosing of 1 mg/kg, administered every other week. Dose may be increased to 3 mg/kg once weekly in patients that do not achieve optimal clinical response
DEA Schedule	Not scheduled
Date of market availability	January 2016
Similar Medications (Look-Alike Sound-Alike)	Selexipag (*Uptravi*), Sitagliptin (*Januvia*)
CLINICAL USE EVALUATION	
Common Adverse Effects	Diarrhea, vomiting, fever, rhinitis, anemia, cough, nasopharyngitis, urticaria, headache, oropharyngeal pain, asthenia, constipation, and nausea
Severe Adverse Effects	Hypersensitivity reactions
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?)	Lipid panel, liver enzymes
Used in Pediatric Areas	Indicated in patients aged 1 month and older. Initiate at 1 mg/kg, and infuse over at least 2 hours
Renal or Hepatic Dosing	None
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindications: None • Warnings and Precautions: - Hypersensitivity reactions, including anaphylaxis, reported as late as 1 year after treatment initiation. Symptoms of hypersensitivity included chest discomfort, tachycardia, tachypnea, dyspnea/severe respiratory distress, generalized/itchy rash, urticaria, swelling of eyelids, rhinorrhea, hyperemia, and conjunctival injection. Pretreatment may prevent subsequent reactions. - Consider risks and benefits of treatment in patients with known systemic hypersensitivity to eggs or egg products
Special administration technique or considerations	• IV infusion only, over a least 2 hours, using a low-protein binding infusion set with an in-line, low-protein binding 0.2 micron filter
Prepared by	Zaynah Ali, Doctor of Pharmacy Candidate 2016

Vonicog alfa (von Willebrand Factor, recombinant) / Vonvendi / Baxalta U.S., Inc.	
Generic Name / Brand Name / Company	Vonicog alfa (von Willebrand Factor, recombinant) / Vonvendi / Baxalta U.S., Inc.
Date of approval	12/8/15
Drug Class (Mechanism of Action if novel agent)	Recombinant von Willebrand factor

Indication	The on-demand treatment and control of bleeding episodes in adults diagnosed with von Willebrand disease
Comparative agent – Therapeutic interchange?	No other recombinant von Willebrand factor only product
Dosage forms/strengths. Common Dose/sig	Injection: lyophilized powder for reconstitution in single-use vials that contain 650 or 1300 IUs of von Willebrand Factor:RCo (VWF:RCo) per vial The initial dosage for minor bleeding episodes is 40 to 50 IU/kg with subsequent doses of 40 to 50 IU/kg every 8 to 24 hours as needed clinically. The initial dosage for major bleeds is 50 to 80 IU/kg followed by subsequent doses of 40 to 60 IU/kg every 8 to 24 hours for 2 to 3 days as needed.
DEA Schedule	Not scheduled
Date of market availability	Latter portion of 2016
Similar Medications (Look-Alike Sound-Alike)	None
CLINICAL USE EVALUATION	
Common Adverse Effects	Pruritus, tachycardia, hypertension, increases in heart rate, ECG T wave inversions, chest discomfort, nausea, infusion site paresthesia, hot flashes, dizziness, dysgeusia, and tremor (all < 1% of infusions)
Severe Adverse Effects	Embolism and thrombosis, hypersensitivity reactions, neutralizing antibody formation and other immunogenicity reactions
Severe Drug-Drug Interactions	None studied/listed, but due to the mechanism of action may interfere with multiple anticoagulant medications
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 levels of VWF:RCo and coagulation factor VIII; monitor for development of von Willebrand factor and factor VIII inhibiting antibodies when suspected
Used in Pediatric Areas	Not studied
Renal or Hepatic Dosing	Not studied
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindicated in patients with a life threatening hypersensitivity reaction to vonicog alfa or any of the constituents included in the product • Thrombotic reactions can occur particularly in patients with known risk factors for thrombosis • Hypersensitivity reactions can occur in association with the use of vonicog alfa • As with all therapeutic proteins, neutralizing antibodies can be produced against vonicog alfa; these antibodies should be monitored for if suspected
Special administration technique or considerations	• Vonicog alfa should be administered immediately after reconstitution, if it cannot be administered right away it may be held at room temperature for up to 3 hours • If a patient is supposed to receive more than 1 vial of solution, the contents of each vial should be drawn up in individual syringes and the syringe left attached to the vial until ready to infuse the product to reduce the risk of contamination • Plastic syringes should be used with vonicog alfa as therapeutic proteins tend to stick to the surface of glass syringes • Vonicog alfa should not be mixed with another other medicinal products
Prepared by	Ross J. Bindler, PharmD

Alectinib / Alecensa / Genentech	
Generic Name / Brand Name / Company	Alectinib / Alecensa / Genentech
Date of approval	12/11/15
Drug Class (Mechanism of Action if novel agent)	Kinase inhibitor
Indication	Anaplastic lymphoma kinase-positive metastatic non-small cell lung cancer. Indicated for use in patients with disease that has progressed on crizotinib or patients who were intolerant to crizotinib.
Comparative agent – Therapeutic interchange?	Ceritinib (Zykadia, Novartis)
Dosage forms/strengths. Common Dose/sig	Capsules: 150 mg Recommended dose: 600mg PO twice daily with food
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Alahist, Alkets, Alosetron, Alustra
CLINICAL USE EVALUATION	
Common Adverse Effects	Fatigue, constipation, edema, myalgia, cough, rash, nausea, headache, diarrhea, dyspnea, back pain, vomiting, increased weight, vision disorder
Severe Adverse Effects	Pulmonary embolism, dyspnea, hyperbilirubinemia, fatal hemorrhage
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?)	Creatine phosphokinase, liver function tests
Used in Pediatric Areas	Safety and efficacy have not been established in the pediatric population.
Renal or Hepatic Dosing	Renal Dosing: In mild to moderate renal impairment, no dosing adjustments are recommended. In severe renal impairment (CrCl < 30 mL/min) or ESRD, no studies have been conducted. Hepatic Dosing: No dosing adjustments are recommended for mild hepatic impairment, defined as total bilirubin less than or equal to the upper limit of normal (ULN) and aspartate transaminase (AST) greater than ULN, **or** total bilirubin greater than 1.0-1.5 time ULN and any AST. In moderate to severe hepatic impairment, no studies have been conducted.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Patients should be warned of the risks and informed of signs and symptoms of: photosensitivity, interstitial lung disease, bradycardia, hepatotoxicity, severe myalgia, and embryo-fetal toxicity. Regular monitoring recommended for hepatotoxicity, bradycardia, and severe myalgia and CPK elevations.
Special administration technique or considerations	Alectinib should be administered with food. Do not open capsules or dissolve capsule contents. Patients should not double doses. The patient should take the next dose at the regularly scheduled time if a dose is missed or lost to vomiting.
Prepared by	Kathleen Nusbaum, Pharm D Candidate 2016

Uridine triacetate / Vistogard / Wellstat Therapeutics Corporation	
Generic Name / Brand Name / Company	Uridine triacetate / Vistogard / Wellstat Therapeutics Corporation
Date of approval	12/11/15
Drug Class (Mechanism of Action if novel agent)	Pyrimidine analog acetylate pro-drug of uridine which is deacetylated by nonspecific esterases yielding uridine in circulation which competitively inhibits the cell damage and death caused by 5-fluorouracil (5-FU)
Indication	Uridine triacetate is indicated for the emergency treatment of adult and pediatric patients following 5-FU or capecitabine overdose or those who exhibit toxicity within 96 hours following the end of 5-FU or capecitabine

	administration; the safety and efficacy of uridine triacetate more than 96 hours following the end of 5-FU or capecitabine administration has not been established
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Oral granules: 10 gram packets. Adults should be administered 10 grams (1 packet) orally every 6 hours for 20 doses. Children should receive 6.2 grams/meter^2 of BSA (not to exceed 10 grams per dose) orally every 6 hours for 20 doses.
DEA Schedule	Not scheduled
Date of market availability	2016
Similar Medications (Look-Alike Sound-Alike)	Uridine triacetate (*Xuriden*)
CLINICAL USE EVALUATION	
Common Adverse Effects	Vomiting, nausea and diarrhea
Severe Adverse Effects	None
Severe Drug-Drug Interactions	None known
Severe Drug-Food Interactions	None, can be administered without regard for meals
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	None
Used in Pediatric Areas	Can be used in pediatric population (see dosing)
Renal or Hepatic Dosing	Not studied
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Use is not recommended for patients not experiencing toxicity as uridine triacetate may diminish the efficacy of 5-FU or capecitabine
Special administration technique or considerations	• For pediatric patients the dose should be measured using either an accurate scale or a graduated teaspoon accurate to ¼ teaspoon • Uridine triacetate should be mixed with 3 to 4 oz of soft foods such as applesauce, pudding or yogurt and ingested within 30 minutes of mixing • If vomiting occurs within 2 hours of dosing another full dose should be administered • If a dose is missed the patient should take the dose as soon as it is remembered and the next dose administered at the scheduled time • Uridine triacetate can be administered via an NG tube or G-tube when necessary • Discard unused granules; do not use granules left in an open packet for a subsequent dose
Prepared by	Ross J. Bindler, PharmD

Sugammadex / Bridion / Merck & Co., Inc.	
Generic Name / Brand Name / Company	Sugammadex / Bridion / Merck & Co., Inc.
Date of approval	12/15/15
Drug Class (Mechanism of Action if novel agent)	Modified gamma cyclodextrin; reduces amount of neuromuscular blocking agent available to bind to nicotinic cholinergic receptors, resulting in reversal of neuromuscular blockade
Indication	Reversal of neuromuscular blockade induced by rocuronium bromide and vecuronium bromide in adult surgery patients
Comparative agent – Therapeutic interchange?	Edrophonium, pyridostigmine
Dosage forms/strengths. Common Dose/sig	Injection: 200mg/2mL (100mg/mL) and 500mg/5mL (100mg/mL) in single-dose vials. Dosing is based on actual body weight. Dosing varies according to the level of spontaneous recovery from neuromuscular blockade. Following rocuronium- or vecuronium-induced neuromuscular blockade: give 4 mg/kg sugammadex if recovery of the twitch response has reached

	1-2 post-tetanic counts (PTC) and there are no twitch responses to train-of-four (TOF) stimulation. Give 2 mg/kg if spontaneous recovery has reached the reappearance of the 2nd twitch in response to TOF stimulation. For rocuronium only: In the case of clinical need to reverse neuromuscular blockade soon after (within 3 minutes) administration of a single dose of 1.2 mg/kg rocuronium, give 16 mg/kg sugammadex.
DEA Schedule	None
Date of market availability	January 2016
Similar Medications (Look-Alike Sound-Alike) that Increase Potential for Error. Tallman lettering?	Bydureon, Brilinta
CLINICAL USE EVALUATION	
Common Adverse Effects	Nausea, vomiting, pain, hypotension, headache
Severe Adverse Effects	Anaphylaxis, hypersensitivity, & marked bradycardia resulting in cardiac arrest
Severe Drug-Drug Interactions	Recovery may be delayed in patients on toremifene. Patients using hormonal contraceptives must use an additional non-hormonal contraceptive for the next 7 days after sugammadex administration.
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?)	None
Used in Pediatric Areas	Safety and efficacy have not been established in the pediatric population.
Renal or Hepatic Dosing	Renal Dosing: In mild to moderate renal impairment, no dosing adjustments are recommended. In severe renal impairment, insufficient safety data exists, and use is not recommended. Hepatic Dosing: Use caution administering sugammadex in patients with hepatic impairment associated with coagulopathy or severe edema.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Avoid use in patients with known hypersensitivity to the sugammadex or any product excipients. Monitor closely for hypersensitivity. Sugammadex should only be administered as a single bolus injection by providers trained in and familiar with characteristics and complications of neuromuscular block reversal agents. Patients must be monitored and supported appropriately until spontaneous respiration is restored and neuromuscular blockade reversal is complete. Patients must be monitored for bradycardia. Significant bradycardia may necessitate administration of anticholinergic agents such as atropine.
Special administration technique or considerations	Administer as an IV bolus. May be administered into the IV line of a running infusion of a compatible fluid; flush between administration of sugammadex and other drugs.
Prepared by	Kathleen Nusbaum, Pharm D Candidate 2016

Selexipag / Uptravi / Actelion Pharmaceuticals Inc.	
Generic Name / Brand Name / Company	Selexipag / Uptravi / Actelion Pharmaceuticals Inc.
Date of approval	12/21/15
Drug Class (Mechanism of Action if novel agent)	Selective non-prostanoid prostacyclin receptor agonist. Selexipag is hydrolyzed by hepatic microsomes to its active metabolite. The active metabolite leads to relaxation of vascular smooth muscle and reduction in peripheral vascular resistance.

Indication	Treatment of pulmonary arterial hypertension (PAH); to delay disease progression and reduce hospitalization risk
Comparative agent – Therapeutic interchange?	Prostanoids; oral treprostinil
Dosage forms/strengths. Common Dose/sig	Oral tablets: 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1000 mcg, 1200 mcg, 1400 mcg, and 1600 mcg Recommended starting dose is 200 mcg twice a day (400 mcg/day), with dose increments of 200 mcg twice daily, at weekly intervals, to highest dose of 1600 mcg twice a day (3200 mcg/day)
DEA Schedule	Not scheduled
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Sebelipase alfa (*Kanuma*), Sitagliptin (*Januvia*)
CLINICAL USE EVALUATION	
Common Adverse Effects	Headache, diarrhea, nausea, vomiting, jaw pain, myalgia, pain in lower extremity, arthralgia, anemia, rash, flushing, and decreased appetite
Severe Adverse Effects	Reduction in hemoglobin to levels below 10 g/dL
Severe Drug-Drug Interactions	Strong CYP2C8 inhibitors increase exposure to selexipag and its active metabolite. Concomitant use with strong CYP2C8 inhibitors is not recommended
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?)	None
Used in Pediatric Areas	Use in this population has not been studied
Renal or Hepatic Dosing	Hepatic Dosing: - No dose adjustment in mild hepatic impairment (Child-Pugh Class A) - Reduce dose to 200 mcg once daily in moderate hepatic impairment (Child-Pugh Class B), and increase dose in 200 mcg increments, at weekly intervals, as tolerated - Avoid use in severe hepatic impairment (Child-Pugh Class C) Renal Dosing - No dose adjustment required in patients with eGFR > 15 mL/min/1.73 m^2 - No recommendations available for patients with eGFR < 15 mL/min/1.73 m^2
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindications: None • Warnings and Precautions: discontinue use in patients exhibiting signs of pulmonary edema, which may be associated with pulmonary veno-occlusive disease (PVOD)
Special administration technique or considerations	• Do not split, crush, or chew tablets • If treatment is missed for 3 or more days, restart at lower dose, and then retitrate
Prepared by	Zaynah Ali, Doctor of Pharmacy Candidate 2016

Lesinurad / *Zurampic* / Ardea Biosciences (AstraZeneca)	
Generic Name / Brand Name / Company	Lesinurad / *Zurampic* / Ardea Biosciences
Date of approval	12/22/15
Drug Class (Mechanism of Action if novel agent)	URAT1 inhibitor that reduces serum uric acid levels by inhibiting reabsorption of uric acid in the kidneys via inhibition of the URAT1 and OAT4 receptors.

Indication	• Treatment of hyperuricemia associated with gout in patients who haven't achieved target serum uric acid levels with a xanthine oxidase inhibitor alone. • Lesinurad is indicated in combination with a xanthine oxidase inhibitor.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Tablets: 200 mg. Recommended dosing is 200 mg once daily (also maximum daily dose), taken in the morning with food and water.
DEA Schedule	Not scheduled
Date of market availability	First quarter 2016
Similar Medications (Look-Alike Sound-Alike)	Lessina, Lescol
CLINICAL USE EVALUATION	
Common Adverse Effects	Reversible increases in serum creatinine levels, headache, influenza, gastroesophageal reflux disease
Severe Adverse Effects	Nephrolithiasis, renal failure
Severe Drug-Drug Interactions	• Increased exposure with CYP2C9 inhibitors (e.g., fluconazole, amiodarone, etc.) and CYP2C9 poor metabolizers • Possible decreased exposure with CYP2C9 inducers (e.g., rifampin, carbamazepine, etc.) • May reduce plasma levels of CYP3A4 substrates (e.g., sildenafil, amlodipine, etc.), resulting in reduced efficacy of these agents. • Aspirin doses higher than 325 mg daily may reduce the effectiveness of lesinurad • Hormonal contraceptives may not be reliable when co-administered. • Epoxide hydrolase inhibitors (e.g., valproic acid), may interfere with lesinurad metabolism and should not be co-administered.
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?)	Serum creatinine, serum uric acid levels
Used in Pediatric Areas	Safety in populations under 18 years of age has not been established
Renal or Hepatic Dosing	• Do not initiate in patients with an estimated CrCl less than 45 mL/min • Increase frequency of monitoring for patients with estimated CrCl between 45 and 60 mL/min. No dose adjustment is necessary. • Discontinue when estimated CrCl falls persistently less than 45 mL/min.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindicated in severe renal impairment (estimated CrCl less than 30 mL/min), end stage renal disease, kidney transplant recipients, patients on dialysis, and Tumor Lysis Syndrome or Lesch-Nyhan Syndrome • Reversible increases in serum creatinine levels have occurred with concomitant use of xanthine oxidase inhibitors • Major adverse cardiovascular events have been observed in clinical trials. A causal relationship has not been established. • The risk of acute renal failure is more common when lesinurad is used without a xanthine oxidase inhibitor.
Special administration technique or considerations	• Should be taken in the morning with food and water • Co-administer with a xanthine oxidase inhibitor • Should be taken at the same time as the morning dose of the xanthine oxidase inhibitor • Patients should remain well hydrated while taking this medication • Gout flare prophylaxis is recommended when starting lesinurad • Gout flares should be managed concurrently with lesinurad use. It does not need to be discontinued.
Prepared by	Justin Buehner, Doctor of Pharmacy Candidate 2016

Bendamustine hydrochloride / Bendeka / Teva Pharmaceuticals	
Generic Name / Brand Name / Company	Bendamustine / Bendeka / Teva Pharmaceuticals
Date of approval	12/7/15
Drug Class (Mechanism of Action if novel agent)	Alkylating agent (nitrogen mustard derivative) with a benzimidazole ring (purine analog)
Indication	Chronic Lymphocytic Leukemia (CLL), Non-Hodgkin Lymphoma (NHL)
Comparative agent – Therapeutic interchange?	• Bendamustine (Treanda) – infused over 30 or 60 minutes • Other comparative agents include other nitrogen mustard agents such as chlorambucil, cyclophosphamide, and ifosfamide • Efficacy relative to other first line therapies other than chlorambucil has not been established in CLL.
Dosage forms/strengths. Common Dose/sig	Injection: 100 mg/4 mL (25 mg/mL) in multiple-dose vials • CLL dosing – 100 mg/m^2 IV over 10 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles • NHL dosing – 120 mg/m^2 IV over 10 minutes on days 1 and 2 of a 21 day cycle, up to 8 cycles.
DEA Schedule	Not Scheduled
Date of market availability	First quarter 2016
Similar Medications (Look-Alike Sound-Alike)	Available as Treanda intravenous (45 mg/0.5 mL and 180 mg/2mL) and Treanda powder for reconstitution (25 mg/vial and 100 mg/vial).
CLINICAL USE EVALUATION	
Common Adverse Effects	• CLL – nausea, vomiting, diarrhea, pyrexia, fatigue, asthenia • NHL – nausea, vomiting, diarrhea, constipation, stomatitis, fatigue, pyrexia, chills, and peripheral edema
Severe Adverse Effects	Myelosuppression, infections, anaphylaxis and infusion reactions, tumor lysis syndrome, skin reactions, extravasation injuries, other malignancies, and fetal harm in pregnant women.
Severe Drug-Drug Interactions	• CYP1A2 inhibitors may increase plasma concentrations of bendamustine and decrease plasma concentrations of active metabolites. • CYP1A2 inducers may increase plasma concentrations of active metabolites and decrease plasma concentrations of bendamustine.
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 CBC with differential and platelets; serum creatinine; ALT, AST, and total bilirubin; potassium; and uric acid levels
Used in Pediatric Areas	• The effectiveness of bendamustine in pediatric patients has not be established. • The safety profile of bendamustine in pediatric patients is consistent with that seen in adults.
Renal or Hepatic Dosing	• Avoid use in patients with estimated CrCl of less than 40 mL/min • Avoid use in patients with moderate (AST/ALT 2.5 – 10 x ULN and total bilirubin 1.5 – 3 x ULN) or severe (total bilirubin > 3x ULN) hepatic impairment
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindicated in patients with known hypersensitivity to bendamustine, polyethylene 400, propylene glycol, or monothioglycerol. • Warnings and Precautions: see Severe Adverse Effects
Special administration technique or considerations	• Dilute with 50 mL of 0.9% sodium chloride, USP; 2.5% dextrose/0.45% sodium chloride, USP; or 5% dextrose, USP. • Administration should be delayed due to Grade 4 hematologic toxicity or clinically significant Grade 2 or greater non-hematologic toxicity.
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