Highlights of FDA Activities – 3/1/16 – 3/31/16

FDA Drug Safety Communications & Drug Information Updates:

Drug Safety Communication: Lack of Sterility Assurance for Human and Animal Sterile Products by I.V. Specialty Ltd. 3/9/16

Following a recent inspection, and observed insanitary conditions, including poor sterile product practices, at the I.V. Specialty facilities, the FDA issued a recommendation for I.V. Specialty to suspend sterile production and implement corrective measures; I.V. Specialty has neither ceased sterile production nor initiated a recall. The FDA has, therefore, issued an alert to healthcare professionals and patients to discontinue use, and quarantine/dispose of all sterile products manufactured or distributed by I.V. Specialty Ltd.

Drug Information Update: Increased Adverse Events with Idelalisib with Other Cancer Medications 3/14/16

The FDA alerted health care professional about reports of increased adverse events, including deaths, with the use of idelalisib (*Zydelig*, Gilead) with other cancer medications. Gilead is discontinuing six clinical trials in patients with chronic lymphocytic leukemia, small lymphocytic lymphoma, and indolent non-Hodgkin lymphomas and is reviewing the findings.

Drug Safety Communication: Potential Risk of Loose Safety Seals on Eye Drops Bottles 3/15/16

The FDA alerted the public about the potential risk from eye drop bottles with loose plastic safety seals, or tamper evident rings, below the bottle cap. The safety seal/tamper evident ring, which should stay connected to the bottle neck, has been slipping off when consumers tilt or squeeze the bottle to place drops into their eyes; six adverse events have been reported. The recommendation is to *not* attempt to remove the safety seal/tamper evident ring, in order to prevent potential contamination of the tip of the dropper. The FDA is in the process of identifying all relevant products, and implementing a change in packaging design.

FDA Drug Safety Communication: FDA Warns About Safety Issues with Opioids 3/22/16

The FDA warned about several safety issues with the opioid class, and new labeling changes for all opioid pain medications to warn of the risks of serotonin syndrome, adrenal insufficiency, and androgen deficiency.

New Safety Measures Announced for Immediate Release (IR) Opioids 03/23/16

The FDA announced class wide safety labeling changes for IR opioid pain medications. These changes include a boxed warning about the serious risks of misuse and abuse, which can lead to addiction, overdose and death, and a change to the approved indication (ie, reserved for pain severe enough to require opioid treatment and for which alternative treatment options (e.g., non-opioid analgesics or opioid combination products, as appropriate) are inadequate or not tolerated).

Major Product Recalls Announced Through MedWatch:

Fluconazole Injection, USP by Sagent: Recall - Impurity Identified 3/1/16

Sagent Pharmaceuticals, Inc. recalled one lot of Fluconazole Injection, USP, in 0.9% Sodium Chloride, 200 mg per 100 mL (Lot 40608) to the hospital/end-user level, due to the presence of an out of specification impurity, identified as metronidazole.

Amikacin Sulfate Injection USP, 1 g/4 mL by Teva: Recall - Glass Particulate Matter 3/9/16

Teva Pharmaceuticals recalled one lot of Amikacin Sulfate Injection, USP, 1 gram/4 mL (250 mg/mL) vials to the end-user level, due to the potential presence of particulate matter, identified as glass, in one vial. Recalled Lot: 4750915 (NDC 0703-9040-01 (individual pack) and NDC 0703-9040-03 (shelf pack)), expiration date 9/2017.

Sodium Bicarbonate Injection, USP by Hospira: Recall - Particulate Matter 3/18/16
Hospira, Inc. recalled one lot of 8.4% Sodium Bicarbonate Injection, USP (NDC: 0409-6625-02, Lot 56-148-EV, Expiry 1AUG2017) at the hospital/retail level due to the presence of a particulate within a single–dose glass flip top vial. The product is packaged 50 mEq (1mEq/mL), 4.2 grams (84 mg/mL), 50mL, Single-dose, packaged 4 boxes of 25 vials per case. The lot was distributed nationwide in the U.S. to wholesalers and hospitals in December 2015.

Compounded Products by Reliable Drug Pharmacy: Recall – Mislabeling and Lack of Quality Assurance 3/24/16
Voluntary recall of all unexpired lots of compounded products distributed between 9/24/15 and 3/24/16 due to concern of lack of quality assurance and potential mislabeling. All recalled products were distributed to patients and veterinarians within California; a few products were distributed to Hawaii, New Mexico, and Michigan.

5% Dextrose Injection USP in PAB by B.Braun Medical Inc: Recall – Leakage & Particulate Matter 3/28/16
B. Braun Medical Inc. recalled to the consumer level one lot of 5% Dextrose Injection USP 100/150 mL container (Lot #J5J706, NDC 0264-1510-32, expires 10/31/2016). Some containers in lot J5J706 exhibited leakage and, in a few instances, visible particulate matter identified to be microbial growth.

Dietary Supplement Recalls & Public Notifications

In March 2016, 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)***
Best Bentonite Clay	Cleansing, Detoxification	Lead
Dynamizm	Weight Loss	Sibutramine
ENVY BP	Weight loss	Sibutramine
Eradicate	Weight Loss	Sibutramine, Desmethylsibutramine
NOW® Andrographis Ext 400 mg 90 VegCaps - Product Code 4591, Lot #1966914*	Supplements	Mislabeled
NOW® Burdock Root 430mg 100 Caps - Product Code 4608, Lot #1969778*	Supplements	Mislabeled
NOW® Cranberry Ext Caps 90 VegCaps Product Code 4632, Lot #1961645*	Supplements	Soy (undeclared allergen)
NOW® Elderberry 500mg 60 VegCaps - Product Code 4667, Lot #1966914*	Supplements	Mislabeled
NOW® Gingko Biloba 60mg 120 VegCaps - Product Code 4687, Lot #1969778*	Supplements	Mislabeled
NOW® Goldenseal Root 500 mg 100 caps Product Code 4692, Lot #1961645*	Supplements	Soy (undeclared allergen)
Propell Platinum	Weight loss	Sibutramine
Salute	Sexual Enhancement	Sildenafil, Thiosildenafil, Sulfoaildenafil
Sextra	Sexual Enhancement	Sildenafil
Xerophagy	Weight Loss	Sibutramine
ZlimXter	Weight Loss and Energy	Sildenafil

*Recalled

New Product Shortages Reported by the FDA:	***Date Initially Posted***
Methylprednisolone Sodium Succinate for Injection, USP (40 mg single dose vial, 125 mg single dose vial)	3/10/16

Product Discontinuations/Withdrawals	***Date Posted***
Enoxaparin sodium injection (300 mg/3 mL vials) The preservative free equivalent, Enoxaparin Sodium Injection in syringe, is still available	3/4/16
Didanosine delayed-release capsules by Mylan (125 mg, 200 mg, 250 mg, and 400 mg) Remains available from other manufacturers	3/11/16
Telithromycin (Ketek®, Sanofi) Tablets (300 mg and 400 mg) No equivalents are available	3/11/16
Rivastigmine tartrate by Sandoz (1.5 mg, 3 mg, 4.5 mg, and 6 mg capsules) Remains available from other manufacturers	3/17/16

New Drug Approvals:	***Description***	***Date Approved***
Coagulation Factor IX (Recombinant)-Albumin Fusion Protein / Idelvion / CSL Behring	See attached drug summary	3/4/16
Antihemophilic Factor VIII (Recombinant)/ Kovaltry / Bayer Healthcare Pharmaceuticals Inc.	Injection to treat hemophilia A in adults and children	3/16/16
Obiltoxaximab/ Anthim / Elusys Therapeutics, Inc	Injection to treat inhalational anthrax (in combination with appropriate antibacterial drugs)	3/18/16
Ixekizumab/ Taltz / Eli Lilly and Co	Injection to treat moderate-to-severe plaque psoriasis; see attached drug summary	3/22/16
Reslizumab / Cinqair / Teva	Intravenous infusion by a healthcare professional for the maintenance treatment of severe asthma in patients aged 18 years and older; see attached drug summary	3/23/16
Defibrotide sodium / Defitelio / Jazz Pharmaceuticals Inc.	Treatment of adult and pediatric patients with hepatic veno-occlusive disease (VOD), also known as sinusoidal obstructive syndrome, with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation (HSCT); see attached drug summary	3/30/16

New Indications:	***Description***	***Date Approved***
Fulvestrant / Faslodex / AstraZeneca	Treatment of hormone receptor positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with palbociclib in women with disease progression after endocrine therapy	3/2/16
Emtricitabine; tenofovir disoproxil fumarate tablets / Truvada / Gilead	Indication expanded to include pediatric patients weighing at least 17 kg; approval also included three new low strength tablets for use in this population	3/10/16
Crizotinib / Xalkori / Pfizer, Inc.	Treatment of ROS-1 positive metastatic non-small cell lung cancer	3/11/16

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Emtricitabine; rilpivirine; tenofovir alafenamide / Odefsey / Gilead	Combination HIV agent containing the new tenofovir salt	3/1/16
Melphalan / Evomela / Spectrum	New propylene glycol-free formulation	3/10/16

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Coagulation Factor IX (Recombinant)-Albumin Fusion Protein / Idelvion / CSL Behring	
Generic Name / Brand Name / Company	Coagulation Factor IX (Recombinant)-Albumin Fusion Protein/Idelvion/CSL Behring
Date of approval	3/4/16
Drug Class (Mechanism of Action if novel agent)	Recombinant coagulation Factor IX-recombinant albumin fusion; fusion process extends the half-life of the fused Factor IX.
Indication	Hemophilia B, for on-demand control and prevention of bleeding, perioperative management of bleeding, and routine prophylaxis
Comparative agent – Therapeutic interchange?	Recombinant factor IX-Fc fusion (Alprolix)
Dosage forms/strengths. Common Dose/sig	Single-use lyophilized powder for reconstitution: 250, 500, 1000, & 2000 IU Factor IX strengths. Administer intravenously (dose/duration is patient-dependent) at room temperature within 4 hours of reconstitution.
DEA Schedule	None
Date of market availability	Expected March 2016
Similar Medications (Look-Alike Sound-Alike)	Coagulation Factor IX (Recombinant)
CLINICAL USE EVALUATION	
Common Adverse Effects	Headache, dizziness, rash, eczema
Severe Adverse Effects	Hypersensitivity
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?)	Plasma Factor IX activity – one-stage clotting assay
Used in Pediatric Areas	Higher dose/kilogram body weight or more frequent dosing may be required due to higher Factor IX body weight adjusted clearance, shorter half-life, and lower recovery in children.
Renal or Hepatic Dosing	No dosage adjustments required
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindicated in patients with a history of life-threatening hypersensitivity to the product or any of its components, including hamster proteins. • Not for immune tolerance induction in patients with Hemophilia B – nephrotic syndrome has been reported in cases when this product was used for immune tolerance induction. • May cause formation of neutralizing antibodies to form. • Thromboembolic complications, including pulmonary embolism, venous thrombosis, and arterial thrombosis, may occur.
Special administration technique or considerations	• Special reconstitution instructions in package insert. • Dilute in Sterile Water for Injection; ensure powder and diluent are at room temperature before reconstituting.
Prepared by	Matthew Iguchi, Doctor of Pharmacy Candidate 2016

Ixekizumab / Taltz / Eli Lilly and Co	
Generic Name / Brand Name / Company	Ixekizumab/ Taltz/ Eli Lilly and Co
Date of approval	3/22/16
Drug Class (Mechanism of Action if novel agent)	Humanized interleukin-17A antagonist; humanized IgG4 monoclonal antibody that selectively binds to a protein (interleukin (IL)-17A) and inhibit the inflammatory response in plaque psoriasis
Indication	Treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy, phototherapy, or a combination of both
Comparative agent – Therapeutic interchange?	Secukinumab
Dosage forms/strengths. Common Dose/sig	Autoinjector or prefilled syringe for injection: 80mg/mL solution Recommended dose: 160 mg (two 80 mg injections) at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks
DEA Schedule	None
Date of market availability	Expected March 2016
Similar Medications (Look-Alike Sound-Alike)	Infliximab, ixazomib, secukinumab, ustekinumab
CLINICAL USE EVALUATION	
Common Adverse Effects	Injection site reactions, upper respiratory tract infections, nausea, fungal (tinea) infections
Severe Adverse Effects	Hypersensitivity reactions (angioedema and urticaria)
Severe Drug-Drug Interactions	Live vaccines should not be given while on treatment; CYP450 substrates
Severe Drug-Food Interactions	None
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Tuberculosis assessment prior to initiation of treatment
Used in Pediatric Areas	Safety and efficacy have not been determined
Renal or Hepatic Dosing	No formal trial of effect of hepatic or renal impairment was conducted
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindicated in patients with history of serious hypersensitivity reaction to ixekizumab or any of the product ingredients. • Infections: affects the immune system and may increase the risk of infection, or an allergic or autoimmune condition • Tuberculosis: evaluate for TB prior to initiating treatment • Inflammatory bowel disease: development or worsening of Crohn's disease and ulcerative colitis have been reported
Special administration technique or considerations	• Inject subcutaneously in the thighs, upper arms, or any quadrant of abdomen • Store in refrigerator between 36°F to 46°F (2°C to 8°C) • Protect from light • Do not freeze or shake injection
Prepared by	Jennifer Nguyen, Doctor of Pharmacy Candidate 2016

Reslizumab / Cinqair / Teva Pharmaceuticals	
Generic Name / Brand Name / Company	Reslizumab / Cinqair / Teva Pharmaceuticals
Date of approval	3/23/16
Drug Class (Mechanism of Action if novel agent)	Humanized interleukin-5 antagonist monoclonal antibody
Indication	Add-on maintenance treatment for severe asthma in patient 18 years and older with eosinophilic phenotype
Comparative agent – Therapeutic interchange?	Nucala (mepolizumab), benralizumab (in development)
Dosage forms/strengths. Common Dose/sig	Dosage form: 100 mg/10 mL (10 mg/mL) solution in single use vials Common dose: 3 mg/kg reslizumab dispensed in an infusion bag of 50 mL 0.9% Sodium Chloride once every 4 weeks administered by IV infusion over 20-50 minutes
DEA Schedule	None
Date of market availability	4/25/16
Similar Medications (Look-Alike Sound-Alike)	Daclizumab
CLINICAL USE EVALUATION	
Common Adverse Effects	Antibody formation (4.8%-5.4%) – clinical relevance unknown; musculoskeletal pain (2.2%); pharyngitis (2.6%)
Severe Adverse Effects	Anaphylaxis (0.3% vs 0% placebo); secondary malignancy (0.6% vs 0.3% placebo)
Severe Drug-Drug Interactions	No known interactions
Severe Drug-Food Interactions	No known interactions
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Pulmonary function tests to assess efficacy; no laboratory monitoring necessary
Used in Pediatric Areas	Not indicated in pediatric patients; studies showed asthma exacerbation rate higher in adolescent patients treated with reslizumab than placebo
Renal or Hepatic Dosing	Specific guidelines are not available; it appears no dosage adjustments are needed
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Do not administer to patients with known hypersensitivity to reslizumab or any of its excipients • Should not be used for acute asthma symptoms or exacerbations • Do not abruptly discontinue systemic or inhaled corticosteroids • It is unknown if reslizumab will influence immune response against parasitic infections; treat patients with pre-existing helminth infections before initiating reslizumab
Special administration technique or considerations	• Dispense proper dose of reslizumab in an infusion bag of 50 mL of 0.9% Sodium Chloride and administer immediately follow preparation – administration not to exceed 16 hours post preparation • Allow dilution to reach room temperature prior to administration • Infuse using in-line, low protein-binding filer (pore size 0.2 micron); reslizumab is compatible with polyethersulfone (PES), polyvinylidene fluoride (PVDF), nylon, and cellulose acetate in-line infusion filters • Infuse over 20-50 minute period depending on total volume per patient weight • Do not infuse concomitantly with other agents; physical and biochemical compatibility studies have not be conducted
Prepared by	Amanda Helmann, Doctor of Pharmacy Candidate 2016

Defibrotide sodium / Defitelio / Jazz Pharmaceuticals	
Generic Name / Brand Name / Company	Defibrotide sodium / Defitelio / Jazz Pharmaceuticals Inc.
Date of approval	3/30/16
Drug Class (Mechanism of Action if novel agent)	Oligonucleotide mixture with profibrinolytic properties with an unclear mechanism of action.
Indication	Treatment of adult and pediatric patients with hepatic veno-occlusive disease (VOD), also known as sinusoidal obstructive syndrome, with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation (HSCT)
Comparative agent – Therapeutic interchange?	None: only proven treatment available for this rare condition
Dosage forms/strengths. Common Dose/sig	Injection: 200 mg/2.5 mL (80 mg/mL) in a single-patient-use vial Dose: 6.25 mg/kg every 6 hours given as a 2-hour intravenous infusion, treat for a minimum of 21 days. If symptoms of VOD have not resolved, continue treatment until resolution or a maximum of 60 days of treatment.
DEA Schedule	None
Date of market availability	April 2016
Similar Medications (Look-Alike Sound-Alike)	Definity
CLINICAL USE EVALUATION	
Common Adverse Effects	Hypotension, diarrhea, vomiting, nausea and epistaxis
Severe Adverse Effects	Hemorrhage, hypersensitivity reaction
Severe Drug-Drug Interactions	May enhance the activity of antithrombotic/fibrinolytic drugs
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 has been established
Renal or Hepatic Dosing	No dosage adjustments required
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindicated: concomitant administration with systemic anticoagulant or fibrinolytic therapy or known hypersensitivity to the product or to any of its excipients • Hemorrhage: monitor patients for bleeding. Withhold or discontinue defibrotide if significant bleeding occurs • Hypersensitivity reactions: if severe or life threatening allergic reaction occurs, discontinue defibrotide, treat according to standard of care, and monitor until signs and symptoms resolve.
Special administration technique or considerations	• Dilute prior to infusion with D5W or NS to a concentration of 4 mg/mL to 20 mg/mL. • Administer by intravenous infusion over a 2-hour period • Administer diluted solution using an infusion set equipped with a 0.2 micron in-line filter. • Flush the intravenous administration line with D5W or NS immediately before and after administration.
Prepared by	Katherine Termath, Doctor of Pharmacy Candidate 2016