Highlights of FDA Activities – 10/1/17 – 10/31/17

FDA Drug Safety Communications & Drug Information Updates:

Intraocular Injections of a Compounded Triamcinolone, Moxifloxacin, and Vancomycin Formulation - A Case of Hemorrhagic Occlusive Retinal Vasculitis (HORV) 10/3/17

The FDA recommended prophylactic intraocular vancomycin, alone or in a compounded combination, not be used during cataract surgery because of the risk of HORV and the lack of adequate controlled studies demonstrating safety and efficacy of intraocular vancomycin in the prevention of endophthalmitis.

Major Product Recalls Announced Through MedWatch:

Intralipid 20% IV Fat Emulsion by Baxter: Recall - Shipment Exposed to Subfreezing Temperatures 10/6/17

One shipment from a single lot of INTRALIPID 20% IV Fat Emulsion, 100 mL, distributed between 8/11/17 and 8/31/17 to hospitals and healthcare providers in the United States, has been recalled to the user level. The product was exposed to subfreezing temperatures during transit to a distribution facility.

Injectable Products by SCA Pharmaceuticals: Recall - Potential Contamination 10/20/17

Various lots of the following products from SCA Pharmaceuticals are recalled to the hospital level due to possible microbial contamination: Succinylcholine chloride 20 mg/mL 10 mL syringe (NDC: 70004-0910-29); hydromorphone 1 mg/mL in 25 mL 0.9% sodium chloride (70004-0303-17); fentanyl 2 mcg/mL + bupivacaine 0.125% in 250 mL 0.9% sodium chloride (70004-0231-40); hydromorphone 20 mcg/mL + bupivacaine 0.075% in 50 mL 0.9% sodium chloride (70004-0331-22); morphine 1 mg/mL in 50 mL 0.9% sodium chloride (70004-0100-22); morphine 1 mg/mL in 100 mL 0.9% sodium chloride (CADD) (70004-0100-63); oxytocin 30 units added to 500 mL Lactated Ringers (70004-0086-44); phenylephrine 100 mcg/mL 10 mL in 12 mL syringe (70004-0810-12); fentanyl citrate 2 mcg/mL + ropivacaine HCl 0.1% (70004-0264-64); calcium gluconate 2 g added to 50 mL 0.9% sodium chloride (70004-0510-30); and rocuronium 10 mg/mL 5 mL in 6 mL syringe (70004-0850-09). Specific lot numbers can be found in the Recall Notice on the FDA site.

Octagam [Immune Globulin Intravenous (human) 10% Liquid Preparation]: Withdrawal 10/23/17

Octapharma USA Inc. is voluntarily recalling Octagam 10% products with lot numbers K724B8541 and K725A8541 after consultation with public health authorities at the FDA.

Dietary Supplement Recalls & Public Notifications

In October, 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)*
A1 Slim*	Weight loss	Sibutramine, phenolphthalein, N-desmethyl sibutramine[1]
Fifty Shades 6000*	Sexual enhancement	Sildenafil, tadalafil, desmethyl carbodenafil[2]
Grande X 5800*	Sexual enhancement	Sildenafil, tadalafil, desmethyl carbodenafil[2]
Papa Zen 3300*	Sexual enhancement	Sildenafil, tadalafil, desmethyl carbodenafil[2]
Rhino 7 Platinum 5000*	Sexual enhancement	Sildenafil, tadalafil, desmethyl carbodenafil[2]
Tiger 5000	Sexual enhancement	Sildenafil, tadalafil[2]

*Recalled

[1]Sibutramine has been associated with increased cardiovascular events; discontinued 2010[FDA]

[2]Sildenafil/tadalafil/vardenafil may interact with nitrates to lower blood pressure to dangerous levels

New Product Shortages Reported by the FDA:	***Date Initially Posted***
Sodium chloride 9% injection bags	10/2/17
Dextrose 5% Injection Bags	10/10/17
Metronidazole injection, USP	10/11/17
Metoclopramide Injection, USP	10/23/17
Guanfacine HCl tablets	10/24/17
Lidocaine HCl and Dextrose Injection Solution – Premix Bags	10/25/17
Hydromorphone HCl Injection, USP	10/31/17

Product Discontinuations/Withdrawals	***Date Posted***
Furosemide tablets (Sandoz): 20 mg, 40 mg, and 80 mg tablets; generics remain available from other manufacturers.	10/5/17
Lisinopril tablets (Sandoz): 2.5 mg, 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg tablets; generics remain available from other manufacturers.	10/5/17
Midodrine tablets (Apotex): 2.5 mg, 5 mg, and 10 mg tablets; generics remain available from other manufacturers	10/16/17
Sumatriptan (ZECUITY®) Iontophoretic Transdermal System (Teva): transdermal discontinued; sumatriptan remains available as subcutaneous injection, oral tablet, nasal spray, and inhalation powder.	10/19/17
Metoclopramide Injection (Teva): discontinued NDC 0703-4502-94; generics remain available from other manufacturers.	10/24/17
Guanfacine tablets (Epic): discontinued 1 mg and 2 mg tablets; generics remain available from other manufacturers.	10/26/17

New Drug Approvals:	***Description***	***Date Approved***
Axicabtagene ciloleucel / Yescarta / Kite Pharma	See attached drug summary	10/18/17
Zoster Vaccine Recombinant, Adjuvanted / Shingrix / GlaxoSmithKline	See attached drug summary	10/20/17
Acalabrutinib / Calquence / AstraZeneca	See attached drug summary	10/31/17

New Indications:	***Description***	***Date Approved***
Onabotulinumtoxin A / Botox Cosmetic / Allergen	Temporary improvement in the appearance of moderate to severe forehead lines associated with frontalis muscle activity	10/3/17
Ustekinumab / Stelara / Janssen	Indication expanded to include adolescents as young as 12 years with moderate-to-severe plaque psoriasis	10/13/17
Golimumab / Simponi Aria / Janssen	Indication expanded to include ankylosing spondylitis and psoriatic arthritis	10/20/17
Rivaroxaban / Xarelto / Janssen	The 10 mg strength is indicated for reducing the continued risk for recurrent venous thromboembolism after completion of at least 6 months of initial anticoagulant therapy	10/27/17

New Dosage Forms or Formulations:	***Description***	***Date Approved***
Triamcinolone acetonide extended-release injectable suspension / Zilretta / Flexion Therapeutics	Intra-articular injection for osteoarthritis knee pain	10/6/17
Pregablin extended-release tablets / Lyrica CR / Pfizer	Once daily tablet for management of diabetic peripheral neuropathic pain and postherpetic neuralgia	10/11/17
Exenatide extended-release injectable suspension / Bydureon Bcise / AstraZeneca Pharmaceuticals LP	Weekly administration with a single-dose autoinjector in patients with type 2 diabetes	10/20/17
Rolapitant injectable emulsion / Varubi / Tesaro	Intravenous infusion for prevention of nausea and vomiting associated with chemotherapy	10/25/17

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New Drug Approvals: Attached Summaries

Axicabtagene ciloleucel / Yescarta / Gilead	
Generic Name / Brand Name / Company	Axicabtagene ciloleucel / Yescarta / Gilead
Date of approval	10/18/17
Drug Class (Mechanism of Action if novel agent)	Autologous T Cell (CAR-T) therapy
Indication	Adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of failed systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma
Comparative agent – Therapeutic interchange?	Tisagenlecleucel (Kymriah); not a therapeutic interchange, each medication is currently FDA approved for different indications, although tisagenlecleucel has also been studied in large B-cell lymphoma
Dosage forms/strengths. Common Dose/sig	Autologous cell suspension for infusion: Suspension of 2 x 10^6 CAR-positive T cells per kg of body weight, with a maximum of 2 x 10^8 CAR-positive viable T cells in approximately 68 mL
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Tisagenlecleucel (Kymriah)
Clinical Use Evaluation	
Common Adverse Effects	>20%: cytokine release syndrome (CRS), fever, hypotension, encephalopathy, tachycardia, fatigue, headache, decreased appetite, chills, diarrhea, febrile neutropenia, infections, nausea, hypoxia, tremor, cough, vomiting, dizziness, constipation, cardiac arrhythmias
Severe Adverse Effects	CRS, neurologic toxicity (including fatal or life-threatening reactions)
Severe Drug-Drug Interactions	None reported
Severe Drug-Food Interactions	None reported
Important Lab Values to assess prior to order entry or at point of clinical follow up.	WBCs (leukocytes, neutrophils), RBCs, thrombocytes, phosphate, sodium, potassium, uric acid, bilirubin, ALT
Used in Pediatric Areas	Not yet established
Renal or Hepatic Dosing	No dosage adjustment necessary
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No contraindications Warnings/precautions • Hypersensitivity reactions: monitor during infusion • Serious infections: monitor patients for signs and symptoms of infection and treat appropriately • Prolonged cytopenias: monitor CBCs for several weeks following infusion since patients may experience prolonged cytopenias up to several weeks • Hypogammaglobulinemia: monitor and provide replacement therapy • Secondary malignancies: contact Kite Pharma • Effects on ability to drive and use machines: advise patients to refrain from driving and engaging in hazardous occupations or activities for at least 8 weeks after infusion
Special administration technique or considerations	• Only administered at approved health institutions who follow a strict REMS criteria • Do not use a leukodepleting filter • Administer a lymphodepleting regimen of fludarabine and cyclophosphamide before infusion • Verify patient's identity prior to infusion

	• Premedicate with acetaminophen and an H1-antihistamine • Confirm availability of tocilizumab prior to infusion
Prepared by	Bryan Huttula, Pharm.D. Candidate 2018
Source	Yescarta (axicabtagene ciloleucel) suspension for intravenous infusion [prescribing information]. Santa Monica, CA: Kite Pharma, Inc.; October 2017.

Zoster Vaccine Recombinant, Adjuvanted / Shingrix / GlaxoSmithKline	
Generic Name / Brand Name / Company	Zoster Vaccine Recombinant, Adjuvanted / Shingrix / GlaxoSmithKline
Date of approval	10/20/17
Drug Class (Mechanism of Action if novel agent)	Recombinant herpes zoster vaccine
Indication	Prevention of herpes zoster (shingles) in adults aged 50 years and older
Comparative agent – Therapeutic interchange?	Zostavax; not an equivalent therapeutic interchange because Shingrix showed higher efficacy rates in all patient populations studied. ACIP recommended Shingrix.
Dosage forms/strengths. Common Dose/sig	Suspension for injection supplied in single dose vial Administer 2 doses (0.5 mL IM each) at 0 and 2 to 6 months
DEA Schedule	None
Date of market availability	May be available by the end of November 2017; ACIP recommendations will be formalized in late 2017 or early 2018.
Similar Medications (Look-Alike Sound-Alike)	Zoster Vaccine Live (Zostavax)
Clinical Use Evaluation	
Common Adverse Effects	Local: pain (78%), redness (38.1%), swelling (25.9%) General: myalgia (44.7%), fatigue (44.5%), headache (37.7%), shivering (26.8%), fever (20.5%), gastrointestinal symptoms (17.3%)
Severe Adverse Effects	Lymphadenitis, fever > 39 C (102.2 F), optic ischemic neuropathy, death, immune-mediated diseases
Severe Drug-Drug Interactions	Immunosuppressive therapies may reduce vaccine effectiveness.
Severe Drug-Food Interactions	None reported
Important Lab Values to assess prior to order entry or at point of clinical follow up.	None reported
Used in Pediatric Areas	Safety and effectiveness in individuals younger than 18 years have not been established. Shingrix is not indicated for prevention of primary varicella infection (chickenpox).
Renal or Hepatic Dosing	No change in dosing
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindication • Hypersensitivity reactions to any component of the vaccine Warning/precaution • Review immunization history for possible vaccine sensitivity and previous adverse reactions related to vaccines • Appropriate medical treatment and supervision must be available prior to administration in the case of an adverse event
Special administration technique or considerations	Requires reconstitution with supplied adjuvant suspension. Must be used immedately or may be stored refrigerated for up to 6 hours. Administer intramuscularly in the deltoid region of the upper arm.
Prepared by	Bryan Huttula, Pharm.D. Candidate 2018
Source	Shingrix (Zoster Vaccine Recombinant, Adjuvanted) Suspension for Intramuscular Injection [prescribing information. Research Triangle Park, NC: GlaxoSmithKline; October 2017.

	Lowes R. ACIP Narrowly Recommends Shingrix for Shingles Over Zostavax. Medscape [Internet]. New York, NY: WebMD; 2017 Oct 25 [cited 2017 Oct 26]. Available from: https://www.medscape.com/viewarticle/887626.

Acalabrutinib / Calquence / AstraZeneca Pharmaceuticals LP	
Generic Name / Brand Name / Company	Acalabrutinib / Calquence / AstraZeneca Pharmaceuticals LP
Date of approval	10/31/17
Drug Class (Mechanism of Action if novel agent)	Bruton tyrosine kinase (BTK) inhibitor
Indication	Treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy
Comparative agent – Therapeutic interchange?	Ibrutinib (Imbruvica) - therapeutic interchange unknown
Dosage forms/strengths. Common Dose/sig	Capsules: 100 mg Common dose/sig: 100 mg orally approximately every 12 hours
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	
Clinical Use Evaluation	
Common Adverse Effects	>20: Anemia, thrombocytopenia, headache, neutropenia, diarrhea, fatigue, myalgia, and bruising
Severe Adverse Effects	Hemorrhage, infection, cytopenias, second primary malignancies, atrial fibrillation and flutter
Severe Drug-Drug Interactions	CYP3A inhibitors and CYP3A inducers: avoid strong inhibitors and inducers; dose adjustments may be necessary with other agents Gastric acid reducing agents: avoid co-administration with proton pump inhibitors; separate dosing with H2 receptor blockers and antacids by 2 hours.
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry or at point of clinical follow up	White blood cells, platelets, and red blood cells monthly
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	No adjustments necessary in mild to moderate renal impairment or hepatic impairment; no information is available to guide dosing in patients with severe renal or hepatic impairment, or end-stage renal disease with dialysis
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications- None Warnings- close monitoring and dose modifications necessary for Grade 3 or greater non-hematologic toxicities, thrombocytopenia, neutropenia lasting longer than 7 days, and with concomitant use with CYP3A inhibitors/inducers and gastric acid reducing agents.
Special administration technique or considerations	Advise patients not to break, open, or chew capsules. Swallow whole capsule with water and with or without food
Prepared by	Mira Kim, Pharm.D. Candidate 2018
Source	Calquence (acalabrutinib) capsules [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2017.