Highlights of FDA Activities – 12/1/14 – 12/31/14

FDA Drug Safety Communications & Drug Information Updates:

FDA Issues Final Rule on Changes to Pregnancy & Lactation Labeling Information for Prescription Drug & Biologic Products – Drug Information Update 12/3/14

The FDA published a final rule setting new standards for how information on medication use in pregnancy and breastfeeding is presented in prescribing information. Three sections labeled "Pregnancy," "Lactation" and "Females and Males of Reproductive Potential" will be included in the prescribing information for all prescription drug and biologic products. The current letter categories for pregnancy risk (A, B, C, D and X) will be replaced with three detailed subsections that describe the risks in terms relating to providing clinical care for pregnant women: "risk summary, " "clinical considerations" and "data." The "Lactation" section will include the same three subsections. Drugs and biologic product applications approved as of June 30, 2015 will be required to use the new format, which will be phased in gradually for previously approved products.

Heart Sync Inc. Multi-function Defibrillation Electrodes: Device Correction – Connector Incompatibility with Philips FR3 and FRx Defibrillator Units 12/3/14

Certain Multi-function Defibrillation Electrodes will not connect with the Philips FR3 and FRx Defibrillator Units. The manufacturer is in the process of revising the labeling to clarify the use of these electrodes. All consumers were notified on 11/11/14 by letter.

CONMED Corporation, PadPro and R2 Multi-Function Defibrillation Electrodes Will Not Work with Philips FR3 and FRx AEDs (Class I Recall) 12/3/14

Since the connector design of the Philips FR3 and FRx AEDs have changed, the CONMED electrodes will no longer work with these AEDs. The FRx AED requires electrode pads be connected to the device before use. The FR3 doesn't require electrode pads to be pre-connected. A delay in the delivering the electrical therapy, leading to serious injury or death, can result if the users don't know that the pads do not work in the FR3 AED. The manufacturer do not recommend the use of the affected electrodes with these 2 AEDs.

Dietary Supplements Containing Live Bacteria or Yeast in Immunocompromised Persons: Warning – Risk of Invasive Fungal Disease 12/9/14

Following last month's reporting of the death of a premature infant administered a dietary supplement as part of an inpatient treatment, and subsequent recall of ABC Dophilus Powder contaminated with Rhizopus oryzae mold, the FDA reminds health professionals that dietary supplements, including those containing live bacteria or yeast, are not generally regulated by the FDA. These products should particularly be used with caution in patients who are immunocompromised. Practitioners wishing to use these products as drugs, to treat, mitigate, cure or prevent a disease or condition, are invited to submit an Investigational New Drug Application (IND) for FDA review. The IND process includes an assessment of the quality of manufacturing and testing. Information on IND submission can be found on the FDA website at
http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/InvestigationalNewDrugINDorDeviceExemptionIDEProcess/default.htm

Ziprasidone Drug Safety Communication – Rare But Potentially Fatal Skin Reactions 12/11/14

Labeling for ziprasidone (Geodon and generics) has been updated to include a new warning regarding the occurrence of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). DRESS may start as a rash and progress to include fever, swollen lymph nodes, and inflammation of the liver, kidney, lungs, heart or pancreas; as well as eosinophilia and potentially death. The FDA has received reports of six patients developing DRESS within 11 and 30 days of initiation of ziprasidone therapy; none of the cases were fatal. Patients should be advised to seek urgent care if they develop fever with rash and/or swollen lymph glands. Health care professionals should immediately discontinue treatment if DRESS is suspected.

IV Solutions from Wallcur of San Diego: CDER Statement – FDA Warns Health Care Professionals Not to Administer These IV Training Products 12/30/14

The FDA alerted health care professionals not to administered IV training products from Wallcur of San Diego in human or animal patients. These products are for training purposes only; serious adverse events have been associated with administration of PractiIV Solution Bags, which are labeled "for clinical simulation."

Major Product Recalls Announced Through MedWatch:

Siemens Healthcare Diagnostics, Rapid Gram Negative Combo Panels – May Produce Incorrect Results (Class I Recall) 12/1/14

This recall includes the Rapid Neg NP Combo Panel Type 3 and Rapid Neg Urine Combo Panel Type 1. These devices, used to identify certain gram negative bacteria and how the bacteria respond to antibiotics in the lab. The recall was issues because incorrect results may occur with aztreonam, cefotaxime, ceftazidime, and ceftriaxone; such as reporting the bacteria is sensitive when it is resistant to the bacteria, leading to ineffective treatment. The manufacturer recommends all consumers to stop using the device and follow recall instructions.

Philips/ Children's Medical Ventures, Gel-E Donut and Squishon 2 – Possibility of Mold (Class I Recall) Updated 12/2/14

This device is used in hospitals, under the supervision of a caregiver, to support and cradle an infant's head and/or body. Since the manufacturer's (Philips Health Care) recall in May 2014, there were new complaints of mold leading to injury. Two different types of molds has been identified and are known to cause serious infections, including skin, eye, sinus, and brain infections. There is a potential that the mold can be transferred to the NICU and PICU. Using this product may cause serious adverse health consequences, including death. The manufacturer recommends all consumers to stop using the device even if there is no visible mold and follow recall instructions.

0.9% Sodium Chloride Injection USP in 100 mL Mini-Bag Plus Container by Baxter: Recall – Particulate Matter 12/16/14

Baxter has recalled two lots (P317842 and P317891) of 0.9% Sodium Chloride Injection USP in 100 mL Mini-Bag Plus containers due to complaints of particulate matter identified as a fragment from the vial adapter.

Mitoxantrone (Hospira): Recall – Subpotency and Out of Specification 12/23/14

Hospira is recalling to the user level 10 lots of mitoxantrone injection distributed for human and veterinary use due to confirmed subpotency and elevated impurity levels. Affected lots were distributed from February 2103 through November 2014; a complete list of affected products can be found in a link on the FDA MedWatch site.

Nellcor Puritan Bennett 980 Ventilator System by Covidien: Class I Recall – Component Failure May Cause Display Failure and Burning Odor 12/31/14

Circuit board in the affected units may have cracks resulting in the display to dim and give off a burning odor. There is no risk of fire, but the part needs to be replaced so that information on the display is visible.

KimVent Microcuff Subglottic Suctioning Endotracheal Tubes by Halyard Health: Class I Recall – Component May Detach During Use 12/31/14

Cuff inflation line on certain endotracheal tubes may detach from the tube during use, which may result in reduced air reaching the lungs. The recall affects units manufactured from 11/15/13 to 10/21/14 and distributed from 12/20/13 to 10/30/14.

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)*
B-Lipo Capsules*	Weight loss	Lorcaserin
SLIM-K Capsules*	Weight loss	Sibutramine, desmethylsibutramine, & phenolphthalein
Triple PowerZEN Gold	Sexual enhancement	Sildenafil
Zhansheng Weige Chaoyue Xilishi	Sexual enhancement	Sildenafil
Samurai-X	Sexual enhancement	Sildenafil

*Recalled

New Drug Shortages Reported by the FDA:	*Date Initially Posted*
Methylphenidate HCl Tablets (Concerta, Janssen)	12/04/14
Phentolamine mesylate Injection, 5 mg (West-Ward)	12/18/14
Quazepam (Doral, Sciecure Pharma) 15 mg – see note below under discontinuations	12/23/14

Product Discontinuations/Withdrawals	*Date Initially Posted*
Gentamicin sulfate injection USP 1.6 mg/mL, 50 mL premix from Hospira	12/02/14
Aripiprazole (Abilify) 1 mg/mL oral solution (NDC 59148-013-15), 10 mg and 15 mg Discmelt orally disintegrating tablets (NDCs 59148-640-23 & 59148-641-23), and 9.75 mg/1.3 mL intramuscular injection (NDC 59148-016-65). Product availability is anticipated through May to November 2015; other Abilify formulations remain available.	12/09/14
Quazepam (Doral) 15 mg tablets / bottle of 100 Meda/Questcor discontinuing production. Generics remain available and Sciecure is planning to bring Doral back to market.	12/17/14

New Drug Approvals:	*Description*	*Date Approved*
Blinatumomab / Blincyto / Amgen Inc.	**See attached drug summary**	12/3/14
Human papillomavirus 9-valent vaccine, recombinant / Gardasil 9 / Merck	HPV vaccine for prevention of 9 types of HPV, compared with the 4 types covered in the current Gardasil product	12/10/14
Finafloxacin otic suspension / Xtoro / Alcon	**See attached drug summary**	12/17/14
Olaparib / Lynparza / AstraZeneca	**See attached drug summary**	12/19/14
Ombitasvir, paritaprevir & ritonavir tablets plus dasabuvir tablets / Viekira Pak / AbbVie	**See attached drug summary**	12/19/14
Ceftolozane-tazobactam / Zerbaxa / Cubist	**See attached drug summary**	12/19/14
Peramivir / Rapivab / Biocryst	**See attached drug summary**	12/19/14
Nivolumab / Opdivo / Bristol-Myers Squibb	**See attached drug summary**	12/22/14

New Indications:	*Description*	*Date Approved*
Ruxolitinib / Jakafi / Incyte Corporation	Polycythemia vera in patients who have had an inadequate response to or are intolerant of hydroxyurea	12/4/14

New Indications continued:	***Description***	***Date Approved***
Aripiprazole / Abilify / Otsuka Pharmaceutical	Tourette's disorder in pediatric patients	12/12/14
Denosumab injection 70 mg/mL / Xgeva / Amgen	Hypercalcemia of malignancy refractory to bisphosphonate therapy	12/5/14
Ramucirumab / Cyramza / Eli LIlly	Use in combination with docetaxel in patients with metastatic non-small cell lung cancer whose disease has progressed during or following treatment with platinum-based chemotherapy	12/17/14
Beclomethasone dipropionate nasal aerosol / Qnasl / Teva	Indication for treatment of nasal symptoms of seasonal and perennial allergic rhinitis expanded to include use in patients 4 through 11 years of age	12/17/14
Elvitegravir + cobicistat + emtricitabine + tenofovir / Stribild / Gilead	For use in HIV-1 infected patients who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure, to replace their current regimen	12/17/14
Gadobutol / Gadavist / Bayer	Use in adults and pediatric patients, including term neonates, for detection and visualization of area with disrupted blood brain barrier and/or abnormal vascularity of the central nervous system	12/29/14
Ivacaftor / Kalydeco / Vertex	Indication expanded to include use in patients with an R117H mutation in the cystic fibrosis transmembrane conductance regulator gene	12/29/14
Spinosad / Natroba / Parapro	Indication expanded to include use for head lice infestations in patients 6 months of age and older	12/30/14

New Dosage Form or Formulation:	***Description***	***Date Approved***
Tobramycin inhalation solution (300 mg/5 mL ampule) + PARI LC PLUS Reusable Nebulizer / Kitabis Pak / Pulmoflow Inc.	Management of cystic fibrosis in adults and pediatric patients 6 years of age and older with *Pseudomonas aeruginosa*	12/2/14
Influenza intradermal quadrivalent vaccine / Fluzone Quadrivalent / Sanofi Pasteur	An intradermal formulation of the quadrivalent vaccine for use in active immunization of persons 18 through 64 years of age for prevention of influenza caused by the influenza A and influenza B viruses containing in the vaccine	12/11/14
Pasireotide injectable suspension / Signifor LAR / Novartis	Treatment of acromegaly in adults for whom surgery is not an option	12/15/14
Lanreotide injection / Somatuline Depot / Ipsen Pharmaceuticals	Treatment of gastroenteropancreatic neuroendocrine tumors in adults with unresectable, well or moderately differentiated, locally advanced or metastatic disease	12/16/14
Ivermectin 1% cream / Soolantra / Galderma	Once-daily topical for the treatment of inflammatory lesions of rosacea; **see attached drug summary**	12/19/14
Liraglutide 3 mg / Saxenda / Novo Nordisk	Once daily injection for chronic weight management in addition to a reduced-calorie diet and exercise; **see attached drug summary**	12/23/14
Diclofenac sodium injection / Dyloject / Javelin Pharms	For the management of mild to moderate pain and management of moderate to severe pain alone or in combination with opioid analgesics; **see attached drug summary**	12/23/14

New Dosage Form or Formulation:	***Description***	***Date Approved***
Memantine HCl extended release + donepezil HCl / Namzaric / Forest Labs	For the treatment of moderate to severe Alzheimer's type dementia in patients stabilized on memantine and donepezil	12/23/14

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Blinatumomab/ Blincyto / Amgen Inc.	
Generic Name / Brand Name / Company	Blinatumomab/ Blincyto / Amgen Inc.
Date of approval	12/3/2014
Drug Class (Mechanism of Action if novel agent)	A bispecific CD19-directed CD3 T-cell engager that activates endogenous T cells when bound to the CD19-expressing target cell on benign and malignant B cells. The drug mediates the formation of a synapse between the T cell and the tumor cell, upregulation of cell adhesion molecules, production of cytolytic proteins, release of inflammatory cytokines, and proliferation of T-cells, resulting in redirected lysis of CD19+ cells.
Indication	Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (R/R ALL)
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Single-use vial: 35 mcg of lyophilized powder for reconstitution One treatment cycle: 4 weeks of continuous IV infusion followed by a 2-week treatment-free interval Patients ≥45 kg: 9 mcg/day on days 1-7 and 28 mcg/day on days 8-28 of the first 42-day cycle. 28 mcg/day on days 1-28 in subsequent cycles. Allow for a minimum of 2 weeks treatment-free between cycles For induction, treatment course is up to 2 cycles For consolidation treatment, 3 additional cycles following induction
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	None
CLINICAL USE EVALUATION	
Common Adverse Effects	Pyrexia, headache, peripheral edema, febrile neutropenia, nausea, hypokalemia, tremor, rash, and constipation
Severe Adverse Effects	Neurologic toxicity, seizures, cytokine release syndrome, febrile neutropenia, pyrexia, pneumonia, sepsis, neutropenia, device-related infection, tremor, encephalopathy, infection, overdose, confusion, Staphylococcal bacteremia, and headache.
Severe Drug-Drug Interactions	CYP450 substrates with a narrow therapeutic index
Severe Drug-Food Interactions	Not reported
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	WBC, ANC, AST, ALT, GGT, total bilirubin
Used in Pediatric Areas	Limited experience
Renal or Hepatic Dosing	No formal pharmacokinetic studies in renal or hepatic impairment.

	No dose adjustments needed for CrCl > 30 mL/min
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Boxed warning: cytokine release syndrome and neurological toxicities • Contraindications: known hypersensitivity to blinatumomab or any component of the product formulation • Monitor patients for signs or symptoms of infection, cytokine release syndrome, infusion reactions, neurological toxicity, and tumor lysis syndrome. • Precautions: infections, tumor lysis syndrome, neutropenia and febrile neutropenia, leukoencephalopathy, and neurologic events such as seizures • Effects on ability to drive and use machines
Special administration technique or considerations	• Follow instructions for preparation and administration to prevent errors • Hospitalization is recommended for the first 9 days of the 1st cycle and first 2 days of the 2nd cycle • Premedicate with dexamethasone 20 mg IV 1 hour prior to the 1st dose of blinatumomab of each cycle, prior to a step dose (i.e. cycle 1 day 8), or when restarting an infusion after ≥4 hours of interruption • Infuse 240 mL blinatumomab IV bag over 24 or 48 hours through a dedicated lumen • Do not flush the infusion line, this can increase the dose
Prepared by	Elaine Cen, Doctor of Pharmacy student, class of 2015

Finafloxacin Otic Suspension / Xtoro / Alcon Labs	
Generic Name / Brand Name / Company	Finafloxacin otic suspension 0.3% / Xtoro / Alcon Labs
Date of approval	December 17, 2014
Drug Class (Mechanism of Action if novel agent)	Otic Antibiotics; fluoroquinolone
Indication	Treatment of acute otitis externa caused by *Pseudomonas aeruginosa* and *Staphylococcus aureus*
Comparative agent – Therapeutic interchange?	Otic ciprofloxacin, otic ofloxacin
Dosage forms/strengths. Common Dose/sig	Otic suspension, 0.3% Instill 4 drops in the affected ear(s) twice daily for 7 days.
DEA Schedule	Not applicable
Date of market availability	Not reported
Similar Medications (Look-Alike Sound-Alike)	Xtandi, ciprofloxacin otic, ofloxacin otic
CLINICAL USE EVALUATION	
Common Adverse Effects	Ear pruritus, nausea
Severe Adverse Effects	None reported
Severe Drug-Drug Interactions	None reported
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry	None
Used in Pediatric Areas	Approved for use in patients 1 year and older; same dose as adults
Renal or Hepatic Dosing	No dosage adjustments necessary
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Allergic reactions may occur in patients allergic to finafloxacin, other product ingredients, or other quinolones • Prolonged use could lead to fungal overgrowth
Special administration technique or considerations	• Warm suspension in hand for 1-2 minutes before instilling • Shake bottle well before use • Lie with affected ear up, instill drops, and maintain position for 60 seconds; repeat in other ear if necessary
Prepared by	Terri Levien, Pharm.D.

Olaparib / Lynparza / AstraZeneca	
Generic Name / Brand Name / Company	Olaparib / Lynparza / AstraZeneca
Date of approval	December 19, 2014
Drug Class (Mechanism of Action if novel agent)	Poly ADP-ribose polymerase (PARP) enzyme inhibitor (targets include PARP1, 2, and 3). Inhibition of PARP enzymes disrupts DNA transcription, cell cycle regulation, and DNA repair; hence, the drug inhibits the growth of cancer cells.
Indication	Monotherapy for BRCA-mutated advanced ovarian cancer in patients previously treated with 3 or more lines of chemotherapy
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Capsules: 50 mg Dose: 400 mg twice daily (i.e., eight 50 mg capsules twice daily) Dose may be decreased to 400 mg per day to diminish adverse events: 200 mg twice daily (i.e., four 50 mg capsules twice daily). It may be further reduced, if necessary, to 200 mg per day: 100 mg twice daily (i.e., two 50 mg capsules twice daily).
DEA Schedule	Not applicable
Date of market availability	Not reported
Similar Medications (Look-Alike Sound-Alike)	None
CLINICAL USE EVALUATION	
Common Adverse Effects	Anemia, nausea, fatigue, asthenia, vomiting, diarrhea, dysgeusia, dyspepsia, headache, decreased appetite, nasopharyngitis/pharyngitis/URI, cough, arthralgia/musculoskeletal pain, myalgia, back pain, dermatitis/rash, and abdominal pain/discomfort commonly occurred in 20% or more of study patients.
Severe Adverse Effects	Myelodysplastic syndrome, acute myeloid leukemia, and pneumonitis were rare, but serious, adverse events reported in study patients.
Severe Drug-Drug Interactions	• Concomitant use with other myelosuppressive anticancer agents increase the possible risk and duration of myelosuppressive toxicity. • Concomitant use with strong CYP3A inhibitors increase olaparib levels by 2.7-fold and with moderate CYP3A inhibitors increases levels by 2-fold. • Concomitant use with strong CYP3A inducers decrease olaparib levels by 87%. Moderate CYP3A inducers are predicted to decrease olaparib levels by 50-60%.
Severe Drug-Food Interactions	Grapefruit and Seville oranges should be avoided.
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	CBC
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	No dose adjustment required for impaired renal function, however patients should be closely monitored for toxicity. No data available for impaired hepatic function as patients with impaired liver function were excluded from study.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• The majority of Myelodysplastic Syndrome/Acute Myeloid Leukemia cases were fatal. Monitor CBC at baseline and every month thereafter. Do not administer drug until patient reaches hematological stability (grade 1 or less) after previous chemotherapy. Interrupt therapy in patients with prolonged hematological toxicity. • Fatal pneumonitis may occur. Monitor for dyspnea, fever, cough, wheezing, or radiological abnormality. Interrupt therapy to investigate and discontinue drug upon positive confirmation of pneumonitis.

	• Avoid use in pregnant women. Olaparib may cause fetal toxicity, as animal studies showed olaparib is teratogenic.
Special administration technique or considerations	Swallow capsules whole; do not chew, dissolve or open capsules. Do not take capsules which appear deformed or show evidence of leakage.
Prepared by	Anne Kim, PharmD, MPH, MIT

Peramivir / Rapivab / Biocryst	
Generic Name / Brand Name / Company	Peramivir injection / Rapivab / Biocryst
Date of approval	December 19, 2014
Drug Class (Mechanism of Action if novel agent)	Influenza virus neuraminidase inhibitor
Indication	Treatment of acute uncomplicated influenza in adults who have been symptomatic for no more than 2 days.
Comparative agent – Therapeutic interchange?	Oseltamivir oral, zanamivir inhalation
Dosage forms/strengths. Common Dose/sig	Injection: 200 mg in 20 mL (10 mg/mL) Dose: 600 mg as an IV infusion over 15 to 30 minutes
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Perampanel, simeprevir
CLINICAL USE EVALUATION	
Common Adverse Effects	Diarrhea
Severe Adverse Effects	Serious skin and hypersensitivity reactions, neuropsychiatric reactions
Severe Drug-Drug Interactions	May diminish efficacy of live attenuated influenza vaccine
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Creatine clearance – to determine renal dosing
Used in Pediatric Areas	Safety and effectiveness have not been established
Renal or Hepatic Dosing	Renal: 200 mg if CrCl 30-49 mL/min, 100 mg if CrCl 10-29 mL/min; in patients on hemodialysis, administered dose after dialysis at dose based on renal function Hepatic: no dosage adjustments necessary
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Efficacy has not been established in patients with serious influenza requiring hospitalization. • Monitor for signs of abnormal behavior, hallucinations, delirium. • Rare cases of serious skin reactions including Stevens-Johnson syndrome and erythema multiforme have been reported with peramivir
Special administration technique or considerations	• Administer as IV infusion over 15 to 30 minutes • Compatible with 0.9% or 0.45% sodium chloride, 5% dextrose, or lactated Ringer's; do not dilute or co-infuse with other medications
Prepared by	Terri Levien, Pharm.D.

Ombitasvir/Paritaprevir/Ritonavir tablets + Dasabuvir tablets / Viekira Pak / AbbVie	
Generic Name / Brand Name / Company	Ombitasvir, paritaprevir, and ritonavir tablets, dasabuvir tablets / Viekira Pak / AbbVie
Date of approval	December 19, 2014
Drug Class (Mechanism of Action if novel agent)	Combination product containing ombitasvir, a hepatitis C virus NS5A inhibitor, paritaprevir, a hepatitis C virus NS3/4A protease inhibitor, ritonavir, a CYP3A inhibitor, and dasabuvir, a hepatitis C virus non-nucleoside NS5B palm polymerase inhibitor
Indication	For use with or without ribavirin for the treatment of patients with genotype 1 chronic hepatitis C virus infection, including patients with compensated cirrhosis. Administered with ribavirin if genotype 1a with or

	without cirrhosis and genotype 1b with cirrhosis; used without ribavirin if genotype 1b without cirrhosis.
Comparative agent – Therapeutic interchange?	Ledipasvir/sofosbuvir (Harvoni, Gilead)
Dosage forms/strengths. Common Dose/sig	Tablets: ombitasvir 12.5 mg, paritaprevir 75 mg, ritonavir 50 mg Tablets: dasabuvir 250 mg Dose: 2 ombitasvir/paritaprevir/ritonavir tablets once daily (in the morning) and one dasabuvir tablet twice daily (morning and evening) with a meal; duration is 12 weeks if genotype 1a or 1b without cirrhosis or genotype 1b with cirrhosis; 24 weeks if genotype 1a with cirrhosis.
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Viagra
CLINICAL USE EVALUATION	
Common Adverse Effects	With ribavirin, greater than 10%: fatigue, nausea, pruritus, other skin reactions, insomnia, asthenia Without ribavirin, 5% or greater: nausea, pruritus, insomnia
Severe Adverse Effects	ALT elevations
Severe Drug-Drug Interactions	Contraindicated with drugs strongly dependent on CYP3A for clearance, strong inducers of CYP3A and CYP2C8, and strong inhibitors of CYP2C8
Severe Drug-Food Interactions	Absorption increased when administered with food
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Liver function tests should be assessed prior to, during the first 4 weeks of therapy, and as clinically indicated thereafter
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	Hepatic: no dosage adjustment in mild impairment (Child-Pugh A); not recommended in moderate impairment (Child-Pugh B); contraindicated in severe impairment (Child-Pugh C). Renal: no dosage adjustment necessary
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Consider ribavirin contraindications, warnings, and precautions if coadministration is necessary • Contraindicated in severe hepatic impairment • Numerous severe drug-drug interactions – consult prescribing information for full list of medications contraindicated with the regimen and requiring use with caution • Contraindicated in patients with known hypersensitivity to ritonavir • ALT elevations were observed in clinical trials and were observed more frequently in female subjects using ethinyl estradiol containing medications. Such medications must be discontinued prior to starting therapy.
Special administration technique or considerations	• Tablets should be taken with a meal, without regard to fat or calorie count
Prepared by	Terri Levien, Pharm.D.

Ceftolozane + Tazobactam / Zerbaxa / Cubist	
Generic Name / Brand Name / Company	Ceftolozane/tazobactam for injection / Zerbaxa / Cubist
Date of approval	December 19, 2014
Drug Class (Mechanism of Action if novel agent)	Combination of a cephalosporin antibacterial and a beta-lactamase inhibitor; demonstrated clinical activity in infections caused by *Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Bacteroides fragilis, Streptococcus anginosus, Streptococcus constellatus,* and *Streptococcus salivarius*.

Indication	Treatment of complicated intra-abdominal infections in combination with metronidazole Treatment of complicated urinary tract infections including pyelonephritis
Comparative agent – Therapeutic interchange?	Meropenem
Dosage forms/strengths. Common Dose/sig	Injection (powder for reconstitution): ceftolozane 1 g/tazobactam 0.5 g Dose: 1.5 g (ceftolozane 1 g/tazobactam 0.5) every 8 hours by IV infusion over 1 hour; treatment duration is 4-14 days in intra-abdominal infections and 7 days in UTIs
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	None
CLINICAL USE EVALUATION	
Common Adverse Effects	5% or greater: nausea, diarrhea, headache, pyrexia
Severe Adverse Effects	Serious hypersensitivity reactions/anaphylaxis; *Clostridium difficile*-associated diarrhea
Severe Drug-Drug Interactions	None reported
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Creatinine clearance to determine if renal dosing is required; monitor daily in patients with changing renal function
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	Renal: CrCl 30-50 mL/min administer 750 mg (500 mg/250 mg) IV every 8 hours; CrCl 15-29 mL/min administer 375 mg (250 mg/125 mg) IV every 8 hours; ESRD on hemodialysis administer 750 mg loading dose followed by 150 mg (100 mg/50 mg) maintenance dose IV every 8 hours Hepatic: no dosage adjustment necessary
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindicated in patients with known serious hypersensitivity to the agent, piperacillin/tazobactam, or other beta-lactam agents • Decreased efficacy in patients with baseline CrCl 30-50 mL/min; monitor renal function and adjust doses as recommended
Special administration technique or considerations	• Administer in conjunction with metronidazole 500 mg IV every 8 hours in treatment of complicated intra-abdominal infections. • Do not mix with other drugs or IV solutions containing other drugs • Vials should be stored refrigerated (2°-8°C, 36°-46°F)
Prepared by	Terri Levien, Pharm.D.

Nivolumab / Opdivo / Bristol-Myers Squibb	
Generic Name / Brand Name / Company	Nivolumab / Opdivo / Bristol-Myers Squibb
Date of approval	December 22, 2014
Drug Class (Mechanism of Action if novel agent)	Programmed death receptor-1 (PD-1) blocking monoclonal antibody
Indication	Treatment of unresectable or metastatic melanoma with disease progression after the use of ipilimumab (Yervoy®) and, if BRAF V600 mutation positive, a BRAF inhibitor
Comparative agent – Therapeutic interchange?	Pembrolizumab (Keytruda®)
Dosage forms/strengths. Common Dose/sig	Available as a 4 mL (40 mg total) and 10 mL (100 mg total) single use vial at a concentration of 10 mg/mL Dose: 3 mg/kg via intravenous infusion over 60 minutes every two weeks until melanoma progression or unacceptable toxicity
DEA Schedule	Not applicable
Date of market availability	Early 2015
Similar Medications (Look-Alike Sound-Alike)	Nabilone, nebivolol, nepafenac, NephPlex®, Optivite®
CLINICAL USE EVALUATION	

Common Adverse Effects	Rash (21%), pruritus (19%), cough (17%), upper respiratory tract infections (11%), peripheral edema (10%)
Severe Adverse Effects	Immune-mediated pneumonitis; immune-mediated colitis; immune-mediated hepatitis; immune-mediated nephritis and renal dysfunction; immune-mediated hypo- and hyperthyroidism; others (pancreatitis, uveitis, demyelination, adrenal insufficiency, hypophysitis, diabetic ketoacidosis, hypopituitarism, Guillain-Barre syndrome, myasthenic syndrome and facial and abducens nerve paresis)
Severe Drug-Drug Interactions	None tested
Severe Drug-Food Interactions	None tested
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	AST, ALT, total bilirubin, serum creatinine, thyroid function tests
Used in Pediatric Areas	Safety and efficacy not established
Renal or Hepatic Dosing	Based on population pharmacokinetic analysis, no adjust will be necessary in adult patients with renal impairment There is no adjustment required in adult patients with mild hepatic impairment based on Child-Pugh score, but has not been studied in adult patients with moderate or severe hepatic impairment
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Immune mediated conditions – pneumonitis, colitis, hepatitis, nephritis, hypo- and hyperthyroidism; treat with corticosteroids based on severity of reaction; withhold or discontinue for severe reactions • Embryofetal toxicity – use contraception while on nivolumab and for at least 5 months after the last dose
Special administration technique or considerations	• Administer over 60 minutes through an intravenous line with a sterile, non-pyrogenic, low protein binding in-line filter of 0.2 to 1.2 micrometers in size • Do not coadminister with other medications • Flush the line after the infusion is complete
Prepared by	Ross Bindler, PharmD

Liraglutide / Saxenda / Novo Nordisk	
Generic Name / Brand Name / Company	Liraglutide / Saxenda / Novo Nordisk
Date of approval	December 23, 2014
Drug Class (Mechanism of Action if novel agent)	Glucagon-like peptide-1 (GLP-1) receptor agonist
Indication	For use as an adjunct to a reduced-calorie diet and an increase in physical activity for chronic weight management in adult patients with a body max index (BMI) of: • 30 kg/m^2 or greater, or • 27 kg/m^2 with at least one weight related comorbid condition
Comparative agent – Therapeutic interchange?	None; not interchangeable with liraglutide for type 2 diabetes (Victoza)
Dosage forms/strengths. Common Dose/sig	Solution for subcutaneous injection in pre-filled, multi-dose pen delivering doses of 0.6, 1.2, 1.8, 2.4, or 3 mg Saxenda should be started at 0.6 mg subcutaneously daily for one week, then increased to 1.2 mg daily for one week, then again increased to 1.8 mg daily for one week, once again increased to 2.4 mg daily for one week and 3 mg daily there-after.
DEA Schedule	Not applicable
Date of market availability	First quarter of 2015
Similar Medications (Look-Alike Sound-Alike)	Sugammadex, liarozole, Lioresal, liraglutide (Victoza)
CLINICAL USE EVALUATION	

Common Adverse Effects	Nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain, and elevations in lipase
Severe Adverse Effects	Hypoglycemia, allergic reactions (anaphylactoid and angioedema), papillary thyroid cancer, colorectal neoplasms, heart conduction disorders, hypotension, abnormalities of various laboratory values including liver enzymes, serum calcitonin, serum lipase and amylase
Severe Drug-Drug Interactions	Liraglutide delays gastric emptying and could impact the absorption of concomitantly administered oral medications. Clinically relevant effects weren't observed in the approval trials; however, caution is advised. Do not use any GLP-1 receptor agonist in combination with Saxenda.
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Blood glucose and HbA_{1c} in patients with type 2 diabetes, serum creatinine
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	Use with caution in patients with mild, moderate or severe renal impairment; there are postmarketing reports of acute renal failure and worsening chronic renal failure with liraglutide. Limited experience with use in patients with mild, moderate or severe hepatic impairment; use with caution.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Risk of thyroid and C-cell tumors • Acute pancreatitis • Acute gallbladder disease • Hypoglycemia with the use of concomitant anti-diabetic agents • Increases in heart rate • Acute renal impairment • Hypersensitivity reactions • Suicidal behavior and ideation
Special administration technique or considerations	• New, unused pens should be stored in the refrigerator at 36 to 46 degrees Fahrenheit. • The pen in use can be stored for 30 days at room temperature. • Remove the cover from the pen and make sure the solution is colorless. • Take a new needle and twist on to the pen until it is tight. • Twist the end of the pen to dial up the correct dose. • Remove the protective cap from the needle and insert into the top layer of the skin. • Press and hold the top button with the dose counter says 0; there may noise or feeling of a click. • Keep the needle in the skin to the count of 6 and then remove the needle from the skin.
Prepared by	Ross Bindler PharmD

Ivermectin 1% cream / Soolantra / Galderma	
Generic Name / Brand Name / Company	Ivermectin 1% cream / Soolantra / Galderma
Date of approval	December 19, 2014
Drug Class (Mechanism of Action if novel agent)	Cream; Avermectin macrocyclic lactone
Indication	Treatment of inflammatory lesions of rosacea
Comparative agent – Therapeutic interchange?	Metronidazole cream
Dosage forms/strengths. Common Dose/sig	Topical cream, 1%, supplied in 30 g, 45 g, and 60 g tubes Apply a pea-size amount to affected areas of the face once daily.
DEA Schedule	Not applicable

Date of market availability	Early 2015
Similar Medications (Look-Alike Sound-Alike)	Ivermectin lotion 0.5%
CLINICAL USE EVALUATION	
Common Adverse Effects	Skin burning sensation, skin irritation
Severe Adverse Effects	None
Severe Drug-Drug Interactions	None
Severe Drug-Food Interactions	None
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 effectiveness not established for this indication.
Renal or Hepatic Dosing	None
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Pregnancy Category C • Ivermectin is excreted in human milk in low concentrations after oral administration; excretion in human milk is unknown after topical administration.
Special administration technique or considerations	• Place pea-size amount on affected area (forehead, chin, nose, and/or each cheek) and then spread as a thin layer, avoiding eyes and lips.
Prepared by	Anne Kim, PharmD, MPH, MIT

Diclofenac Sodium Injection / Dyloject / Javelin Pharms	
Generic Name / Brand Name / Company	Diclofenac sodium / Dyloject / Javelin Pharms
Date of approval	December 23, 2014
Drug Class (Mechanism of Action if novel agent)	NSAID
Indication	Management of mild to moderate pain; management of moderate to severe pain alone or with opioid analgesics
Comparative agent – Therapeutic interchange?	Ketorolac injection, Ibuprofen injection
Dosage forms/strengths. Common Dose/sig	37.5 mg/mL single-dose vial Inject 37.5 mg via intravenous bolus injection over 15 seconds every 6 hours as needed – not to exceed 150 mg/day.
DEA Schedule	Not applicable
Date of market availability	Not reported
Similar Medications (Look-Alike Sound-Alike)	Dolgic, Dylix, Dilex
CLINICAL USE EVALUATION	
Common Adverse Effects	Gastrointestinal reactions (abdominal pain, constipation, diarrhea, dyspepsia, flatulence, gross bleeding/perforation, heartburn, nausea, GI ulcers, vomiting), abnormal renal function, headache, infusion site pain, dizziness, insomnia, pruritus, hypotension
Severe Adverse Effects	Anaphylaxis, hypersensitivity reactions, severe skin reactions (Stevens-Johnson Syndrome, toxic epidermal necrolysis, exfoliative dermatitis)
Severe Drug-Drug Interactions	Concomitant administration with: - aspirin decreases the protein binding of diclofenac. - anticoagulants (e.g., warfarin) increases risk of gastrointestinal bleeding. - ACE inhibitors decreases the antihypertensive effect of ACE inhibitors. - cyclosporine increases risk of cyclosporine nephrotoxicity. - diuretics decreases natriuretic effect of furosemide and thiazides. - lithium increases risk of lithium toxicity due to decreased renal clearance of lithium. - methotrexate increases risk of methotrexate toxicity. - CYP2C9 inhibitors increases diclofenac levels.

	- CYP2C9 inducers decreases diclofenac levels.
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Monitor for signs or symptoms of gastrointestinal bleeding. Monitor CBC, liver enzymes, and basic chemistry panel
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	No dose adjustment required for mild hepatic impairment or mild to moderate renal impairment. Use in patients with moderate to severe hepatic impairment is not recommended, and use in moderate to severe or severe renal impairment should be avoided.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Gastrointestinal – inflammation, bleeding, ulceration, perforation of gastrointestinal tract • Hepatic – elevated liver enzymes, hepatotoxicity, jaundice, liver necrosis, liver failure • Hematological – anemia, increased bleeding time from inhibition of platelet aggregation • Hypertension – increased risk of new onset or worsening of pre-existing hypertension • Renal – avoid use in patients with moderate to severe renal insufficiency • Anaphylaxis – avoid use in patients with known hypersensitivity to diclofenac • Cardiovascular – avoid use in patients with perioperative pain in the setting of coronary artery bypass graft surgery to avoid increased risk of cardiovascular thrombotic events, myocardial infarction, or stroke • Asthma – avoid use in aspirin-sensitive asthma patients, use with caution in patients with pre-existing asthma • Pre-existing congestive heart failure/edema – use with caution because drug may increase fluid retention and edema • Masking inflammation/fever – infections may not be detected since diclofenac decreases signs of fever and inflammation • Wound healing – caution with post-operative use because drug may deter wound healing • Pregnancy Category C prior to 30 weeks gestation; Category D starting at 30 weeks gestation – avoid use at 30 weeks gestation and beyond to prevent premature closure of the fetal ductus arteriosus
Special administration technique or considerations	• Patient should be well-hydrated prior to drug administration.
Prepared by	Anne Kim, PharmD, MPH, MIT