Highlights of FDA Activities – 7/1/15 – 7/31/15

FDA Drug Safety Communications & Drug Information Updates:

Codeine Cough-and-Cold Medicines in Children: FDA Evaluating Potential Risk of Serious Side Effects 7/1/15
The FDA is investigating the safety of codeine-containing medicines in the treatment of coughs and colds in children because of the potential for serious respiratory side effects, particularly in children with preexisting respiratory problems. Parents and caregivers should be advised to stop giving their child codeine and seek medical attention immediately if they observe any signs of slow or shallow breathing, difficult or noisy breathing, confusion, or unusual sleepiness in their child. Health care professionals should use caution when prescribing or recommending codeine-containing cough-and-cold medicines to children.

Unapproved Prescription Otic Products: Safety Alert - Not FDA Evaluated for Safety, Effectiveness and Quality 7/1/2015
The FDA has initiated enforcement action against companies that manufacture and/or distribute certain unapproved prescription ear drop products labeled to relieve ear pain, infection, and inflammation. The unapproved prescription ear drops contain active ingredients such as benzocaine and hydrocortisone, and have not been evaluated by the FDA for safety, effectiveness and quality.

FDA Warns of Counterfeit Diazepam 7/6/2015
The FDA warned consumers purchasing diazepam online that counterfeit diazepam, which was actually haloperidol, has resulted in 700 adverse events in patients in Central Africa who took the mislabeled medication. There are no reports that the product has entered the United States, but the FDA advises patients purchasing diazepam online to validate the authenticity of the product. The counterfeit tablets are light yellow and scored on one side, with the imprint AGOG on the unscored side.

NSAIDs (non-aspirin): FDA Strengthens Warning of Increased Chance of Heart Attack or Stroke 7/9/15
The FDA is strengthening an existing label warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) increase the risk of a heart attack or stroke. The FDA is requiring updates to the drug labels of all prescription NSAIDs. Patients and health care professionals should remain alert for heart-related side effects the entire time that NSAIDs are being taken. Patients taking NSAIDs should seek medical attention immediately if they experience symptoms such as chest pain, shortness of breath or trouble breathing, weakness in one part or side of their body, or slurred speech.

Adverse Events with use of LARIAT Suture Delivery Device for Left Atrial Appendage Closure 7/13/15
The FDA alerted health care professionals and patients of reports of patient deaths and serious adverse events associated with the use of the LARIAT device to deliver a suture to close the left atrial appendage to prevent stroke in patients with atrial fibrillation. The safety and effectiveness of the device has not been established for this use, and the potential risks and benefits must be careful considered. To date the FDA has identified 45 adverse events associated with this use of the device, including 6 deaths and 34 events requiring emergency heart surgery.

Proglycem (diazoxide): Reports of Pulmonary Hypertension in Infants and Newborns 7/16/15
The FDA is warning that pulmonary hypertension has been reported in infants and newborns treated with Proglycem (diazoxide) for low blood sugar. In all cases, the pulmonary hypertension resolved or improved after diazoxide was stopped. The FDA investigation is ongoing and will determine whether changes are needed in the prescribing information. Parents and caregivers of any child receiving Proglycem should be advised to watch for signs of difficulty breathing such as flaring nostrils, grunting, unusual movement of their child's chest, rapid breathing, difficulty feeding, or a bluish color of the lips or skin.

Gadolinium-based Contrast Agents for Magnetic Resonance Imaging (MRI): FDA Evaluating the Risk of Brain Deposits With Repeated Use 7/27/15

The FDA is investigating the risk of brain deposits following repeated use of gadolinium-based contrast agents (GBCAs) for magnetic resonance imaging (MRI). Recent publications in the medical literature have reported that deposits of GBCAs remain in the brains of some patients who undergo four or more contrast MRI scans, long after the last administration. It is unknown whether these gadolinium deposits are harmful or can lead to adverse health effects. At this time no labeling changes have been recommended, but the FDA advised health care professional to limit GBCA use to clinical circumstances where it is necessary and to reassess the use of repeated GBCA MRIs.

Brintellix (vortioxetine) and Brilinta (ticagrelor): Name Confusion 7/30/15

The FDA is warning health care professionals and patients that reports of confusion between the brand names of the antidepressant Brintellix and anti-blood clotting medication Brilinta have resulted in the wrong medication being prescribed or dispensed. Ingestion of the wrong medication as a result of an error has not been reported; however, reports of prescribing and dispensing errors continue. Health care professionals can reduce the risk of name confusion by including the generic name of the medication, in addition to the brand name, and the indication for use when prescribing these medications. Patients should check their prescriptions to ensure that the correct medication was dispensed.

Symbiq Infusion System by Hospira: Cybersecurity Vulnerabilities 7/31/15

Cybersecurity vulnerabilities have been identified with the Symbiq Infusion System that could allow unauthorized access to the device remotely through a hospital network. Although no instances have been identified of an unauthorized party gaining access to a device, the FDA strongly encourages health care facilities to discontinue use of these devices.

Major Product Recalls Announced Through MedWatch:

FLOW-i Anesthesia Systems by Maquet: Class I Recall - Dislodged Patient Cassette May Stop Patient Ventilation 7/1/15

The FLOW-i Anesthesia Systems by Maquet has been recalled following receipt of several complaints where patient cassettes, which are the center of gas flow in the system, have come loose. The patient cassette locking device may accidentally release the patient cassette from its mount when users perform a change of system. This may cause anesthesia gas to leak and could prevent the ventilator from providing breathing support if not corrected immediately.

Lifesaver Single Patient Use Manual Resuscitator by Teleflex Hudson RCI: Class I Recall - Intake Port Blockage 7/2/15

The oxygen intake port may be blocked, which can prevent the bag from filling. This may prevent the device from delivering breathing support to the patient.

Calcium Chloride Intravenous Infusion 10% w/v 10 mL Prefilled Syringe by Mylan: Market Withdrawal – Difficulties in Administration 7/14/15

Mylan reissued an advisory regarding withdrawal of calcium chloride prefilled syringes used in emergency situations, following reports of difficulties in administration. A complete list of affected lots can be found at: http://www.fda.gov/Safety/Recalls/ucm454770.htm. Inventory and crash kits should be checked, and any recalled product quarantined.

0.9% Sodium Chloride Injection, USP, 50mL and 100mL by Baxter: Recall - Particulate Matter 7/20/15

Baxter International Inc. announced it is voluntarily recalling two lots of IV solutions due to the potential presence of particulate matter. The particulate matter in each case was determined to be an insect and was identified as a result of a customer complaint. The matter was identified prior to patient administration and there have been no adverse events associated with this issue reported to Baxter. This recall affects Lot Numbers P319921 and P327635.

Major Product Recalls Announced Through MedWatch (continued…)

Sterile Human and Veterinary Compounded Drugs by Moses Lake Professional Pharmacy: Recall - Lack of Sterility Assurance 7/27/15

Moses Lake Professional Pharmacy recalled human and veterinary sterile compounded drugs to the consumer level due to lack of sterility assurance. The company has not received any reports of product contamination or adverse events to date, but issued the recall following a recent inspection which identified an issue with sterility assurance. The recalled products were made from 7/21/2014 through 7/21/2015, and dispensed to patients or distributed to physicians for further administering to patients in the states of Arizona, Idaho, Florida, Oregon, Texas, and Washington.

Adrucil (fluorouracil injection, USP) 5 g/100 mL (50 mg/mL) by Teva Parenteral Medicines: Recall - Particulate Matter 7/27/15

Teva recalled six lots of Adrucil (fluorouracil injection, USP) 5 g/100 mL (50 mg/mL; 100 mL vials packaged individually NDC 0703-3019-11 or in cartons of 5 vials NDC 0703-3019-12) due to the potential presence of particulate matter identified as aggregate of silicone rubber pieces from a filler diaphragm and fluorouracil crystals. A complete list of lot numbers can be found at: http://www.fda.gov/Safety/Recalls/ucm456093.htm

Hydrochlorothiazide tablets 25 mg by Unichem Pharmaceuticals: Recall – Potential Presence of Foreign Tablets 7/31/15

Unichem issued a recall to the consumer level for one lot of 1000-count bottles of hydrochlorothiazide 25 mg tablets (Lot# GHYL15028; Exp. April 2018) due to identification of a clopidogrel tablet in a bottle.

0.9% Sodium Chloride injection, USP from Baxter International: Recall – Potential for Leaking Containers, Particulate Matter, and Missing Port Protectors 7/31/15

Baxter issued a recall to the user level for one lot of 0.9% Sodium Chloride injection, USP (NDC 0338-0049-03; Lot# C964601, Exp. 04/30/2016) following reports of leaking containers, particulate matter, and missing port protectors.

Dietary Supplement Recalls & Public Notifications

In July, 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)*
Akttive High Performance Fat Burner Gold Capsules*	Weight loss	Sibutramine, desmethylsibutramine, phenolphthalein
Zero Xtreme Capsules	Weight loss	Sibutramine and desmethylsibutramine

*Recalled

New Product Shortages Reported by the FDA:	*Date Initially Posted*
Sacrosidase (Sucraid) Oral Solution	7/9/15
Levetiracetam (Keppra) Injection	7/22/15
Cefepime Injection	7/22/15

Product Discontinuations/Withdrawals	*Date Posted*
Morphine sulfate extended-release capsules (Avinza, King Pharmaceuticals)	7/13/15

New Drug Approvals:	*Description*	*Date Approved*
Lumacaftor+ivacaftor / Orkambi / Vertex	See attached drug summary	7/2/15
Sacubitril+valsartan / Entresto / Novartis	See attached drug summary	7/7/15
Brexpiprazole / Rexulti / Otsuka Pharm	See attached drug summary	7/10/15
Alirocumab / Praluent / Sanofi-Regeneron	See attached drug summary	7/24/15
Daclatasvir / Daklinza / Bristol-Myers Squibb	See attached drug summary	7/24/15
Sonidegib / Odomzo / Novartis	See attached drug summary	7/24/15

New Indications:	***Description***	***Date Approved***
Gefitinib / Iressa / AstraZeneca	First-line treatment of patients with metastatic non-small cell lung cancer with tumors expressing EGFR exon 19 deletions or exon 21 substitution mutations	7/13/15
AnobobutulinumtoxinA / Dysport / Ipsen Biopharmaceuticals	Treatment of upper limb spasticity in adults	7/15/15
Carfilzomib / Kyprolis / Onyx Pharmaceuticals	Use in combination with lenalidomide and dexamethasone for the treatment of patients with relapsed multiple myeloma who have received 3 prior lines of therapy	7/24/15

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Tacrolimus / Envarsus XR / Veloxis Pharma Inc.	Extended release tablet for prophylaxis of organ rejection in kidney transplant recipients initially treated with tacrolimus immediate-release formulations	7/10/15
Adapalene 0.3% & benzoyl peroxide 2.5% gel / Epiduo Forte / Galderma	Topical gel for the treatment of acne vulgaris	7/15/15
Ombitasavir + Paritaprevir + Ritonavir / Technivie / Abbvie Inc.	Fixed dose combination for the treatment of patients with genotype 4 chronic hepatitis C infection without cirrhosis	7/24/15
Azelaic acid 15% foam / Finacea / Bayer	Topical foam for the treatment of inflammatory papules and pustules of mild to moderate rosacea	7/29/15

Compiled by:

Terri Levien, Pharm.D.
Ross Bindler, Pharm.D., PGY1 Drug Information Resident
Anne Kim, Pharm.D., PGY1 Drug Information Resident
Kalvin Stoker, Pharm.D. Candidate 2016

Drug Information Center
College of Pharmacy
Washington State University
PO Box 1495
Spokane, WA 99210-1495
(509) 358-7662
Pharmacy.druginfo@wsu.edu

Lumacaftor+Ivacaftor / Orkambi / Vertex	
Generic Name / Brand Name / Company	Lumacaftor+Ivacaftor / Orkambi / Vertex
Date of approval	July 2, 2015
Drug Class (Mechanism of Action if novel agent)	Cystic Fibrosis Transmembrane conductance Regulator (CFTR) potentiator. Lumacaftor improves the conformational stability of F508del-CFTR, resulting in increased processing and trafficking of mature protein to the cell surface. Ivacaftor is a CFTR potentiator that facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the CFTR protein at the cell surface.
Indication	Patients >12 years with homozygous *F508del* mutation in the CFTR gene (safety and efficacy have not been established in CF patients other than those homozygous for the *F508del* mutation)
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Tablets: lumacaftor 200 mg & ivacaftor 125 mg. Dose: 2 tablets orally every 12 hours with a fat-containing food
DEA Schedule	Not applicable
Date of market availability	Available

Similar Medications (Look-Alike Sound-Alike)	Ivacaftor
CLINICAL USE EVALUATION	
Common Adverse Effects	Dyspnea, nasopharyngitis, nausea, diarrhea, upper respiratory tract infections, fatigue, abnormal respiration, rash, flatulence, rhinorrhea, increased blood creatine phosphokinase
Severe Adverse Effects	Hemoptysis, cough, worsening liver function, hepatic encephalopathy, increased blood creatine phosphokinase, bilirubin and transaminases, cataracts, and pneumonia
Severe Drug-Drug Interactions	• No dose adjustment necessary when CYP3A4 inhibitors are initiated in patients already taking lumacaftor/ivacaftor. • When initiating lumacaftor/ivacaftor in patients taking strong CYP3A4 inhibitors, reduce initial dose to 1 tablet daily for the first week to achieve steady-state induction effect of lumacaftor. • Co-administration with strong CYP3A inducers, such as rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort, is not recommended. • Co-administration with sensitive CYP3A substrates and CYP3A substrates with a narrow therapeutic index is not recommended. • Hormonal contraceptives should not be relied upon as an effective method of contraception when co-administered with lumacaftor/ivacaftor. • Lumacaftor/ivacaftor may reduce the exposure and effectiveness of many other medications including montelukast, systemic corticosteroids, antibiotics, antifungals, ibuprofen, antidepressants, oral hypoglycemics, proton pump inhibitors, and warfarin.
Severe Drug-Food Interactions	N/A
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	ALT, AST, and bilirubin should be assessed prior to initiating lumacaftor/ivacaftor, every 3 months during the first year of treatment, and annually thereafter. For patients with a history of ALT, AST, or bilirubin elevations, more frequent monitoring should be considered
Used in Pediatric Areas	Safety and efficacy have not been established in patients younger than 12 years.
Renal or Hepatic Dosing	No dose adjustment is necessary for patients with mild hepatic impairment (Child-Pugh Class A). A dose reduction to 2 tablets in the morning and 1 tablet in the evening is recommended for patients with moderate hepatic impairment (Child-Pugh Class B). Studies have not been conducted in patients with severe hepatic impairment (Child-Pugh Class C); the dose should not exceed 1 tablet twice daily in patients with severe hepatic impairment. Lumacaftor/ivacaftor has not been studied in patients with mild, moderate, or severe renal impairment or in patients with end-stage renal disease.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Use with caution in advanced liver disease; monitor closely. • Closely monitor patients with FEV1 < 40% predicted. • Monitor for cataracts.
Special administration technique or considerations	• Lumacaftor/ivacaftor is best absorbed when taken with fat-containing foods (eggs, avocados, nuts, butter, cheese pizza, whole-milk dairy products.).
Prepared by	Kalvin Stoker, WSU PharmD candidate, 2016

Sacubitril + valsartan / Entresto / Novartis Pharmaceuticals

Generic Name / Brand Name / Company	Sacubitril + valsartan / Entresto / Novartis Pharmaceuticals
Date of approval	July 7, 2015
Drug Class (Mechanism of Action if novel agent)	Combination neprilysin inhibitor, sacubitril, and angiotensin receptor blocker, valsartan. Sacubitril inhibits neprilysin (neutral endopeptidase; NEP) via LBQ657, the active metabolite of the prodrug sacubitril, resulting in increased levels of peptides degraded by neprilysin, such as natriuretic peptides.
Indication	To reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Tablets: sacubitril 24 mg/valsartan 26 mg, sacubitril 49 mg/valsartan 51 mg, sacubitril 97 mg/valsartan 103 mg Recommended starting dose sacubitril 49 mg/valsartan 51 mg twice daily, increasing after 2-4 weeks to the target dose of valsartan 97 mg/valsartan 103 mg twice daily. Reduced starting dose recommended in patients not taking an ACE inhibitor or ARB or previously taking low doses of these agents.
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Valsartan
CLINICAL USE EVALUATION	
Common Adverse Effects	Hypotension, hyperkalemia, cough, dizziness, renal failure
Severe Adverse Effects	Impaired renal function, angioedema, hyperkalemia
Severe Drug-Drug Interactions	Avoid use with an ACE inhibitor or ARB Potassium-sparing diuretics: may increase serum potassium NSAIDS: may increase risk of renal impairment Lithium: increased risk of lithium toxicity Aliskiren : avoid in patients with diabetes
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 and potassium should be monitored periodically.
Used in Pediatric Areas	Safety and effectiveness in pediatric patients have not been established.
Renal or Hepatic Dosing	A starting dose of sacubitril 24 mg/valsartan 26 mg twice-daily is recommended for patients with moderate hepatic impairment (Child-Pugh B classification) or severe renal impairment (eGFR <30 mL/min/1.73 m^2). Avoid use in severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications • hypersensitivity to any component • history of angioedema related to ACE inhibitor or ARB • concomitant use with ACE inhibitors • concomitant use with aliskiren in patients with diabetes Warnings • Monitor for angioedema and hypotension • Monitor renal function and potassium • Discontinue during pregnancy
Special administration technique or considerations	• Advise patients to discontinue use of previous ACE inhibitor or ARB. Allow 36 hour wash-out period if switching from or to an ACEI.
Prepared by	Kalvin Stoker, WSU PharmD candidate, 2016

Brexpiprazole / Rexulti / Otsuka Pharm

Generic Name / Brand Name / Company	Brexpiprazole / Rexulti / Otsuka Pharm
Date of approval	July 10, 2015
Drug Class (Mechanism of Action if novel agent)	Atypical antipsychotic
Indication	• Treatment of Schizophrenia • Adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD)
Comparative agent – Therapeutic interchange?	aripiprazole
Dosage forms/strengths. Common Dose/sig	Oral Tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg Major Depressive Disorder dosing: Recommended starting adjunctive treatment is 0.5 mg or 1 mg daily. Target daily dose of 2 mg. Titration increases should occur at weekly intervals with maximum recommended daily dose of 3 mg. Schizophrenia dosing: Recommended starting dose of 1 mg daily for 4 days with targeted daily dose of 2 mg to 4 mg. Maximum recommended daily dose is 4 mg.
DEA Schedule	Not applicable
Date of market availability	August 2015
Similar Medications (Look-Alike Sound-Alike)	None identified
CLINICAL USE EVALUATION	
Common Adverse Effects	Weight gain, akathisia, headache, fatigue
Severe Adverse Effects	EPS, dystonia, angioedema, anaphylaxis
Severe Drug-Drug Interactions	Strong CYP3A4 inhibitors (ie., Itraconazole, ketoconazole)- reduce brexpiprazole dose Strong CYP2D6 inhibitors (ie., paroxetine, fluoxetine)- reduce brexpiprazole dose Strong CYP3A4 inducers (ie., rifampin)- increase brexpiprazole dose Additional dose reductions in known CYP2D6 poor metabolizers
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?)	Periodic monitoring of blood glucose and lipids advised; CBC recommended in patients with pre-existing low white blood cell count or history of leukopenia or neutropenia
Used in Pediatric Areas	Safety and effectiveness in pediatric patients have not been established
Renal or Hepatic Dosing	For patients with moderate, severe or end-stage renal impairment (CrCl <60 mL/minute), the maximum recommended dosage is 2 mg once daily for patients with MDD and 3 mg once daily for patients with schizophrenia. For patients with moderate to severe hepatic impairment (Child-Pugh score ≥7), the maximum recommended dosage is 2 mg once daily for patients with MDD, and 3 mg once daily for patients with schizophrenia.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications • Known hypersensitivity to any product components Warnings • Increased mortality and cerebrovascular adverse reactions in elderly patients with dementia-related psychosis • Suicidal thoughts and behaviors • Neuroleptic Malignant Syndrome • Tardive dyskinesia • Metabolic changes (hyperglycemia, dyslipidemia, weight gain) • Leukopenia, neutropenia, agranulocytosis • Orthostatic hypotension and syncope • Seizures

	• Body temperature dysregulation • Dysphagia • Potential for cognitive motor impairment
Special administration technique or considerations	May be taken with or without regard to food
Prepared by	Kalvin Stoker, WSU PharmD candidate, 2016

Alirocumab / Praluent / Sanofi-Regeneron	
Generic Name / Brand Name / Company	Alirocumab / Praluent / Sanofi-Regeneron
Date of approval	July 24, 2015
Drug Class (Mechanism of Action if novel agent)	Antihyperlipidemic agents; Proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor. Alirocumab inhibits the binding of PCSK9 to LDL receptors, thereby increasing the number of LDL receptors available to clear LDL and lowering LDL-C levels.
Indication	Adjunct to diet and maximally tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional LDL-C lowering
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Injection: 75 mg/mL or 150 mg/mL in single-dose prefilled pen or syringe Dose: 75 mg subcutaneously once every 2 weeks; if inadequate LDL-C lowering the dose may be increased to a maximum of 150 mg every 2 weeks
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	None identified
CLINICAL USE EVALUATION	
Common Adverse Effects	Nasopharyngitis, injection site reactions, influenza
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?)	LDL-C levels should be measured 4 to 8 weeks after initiating therapy to assess response and determine need for dosage adjustment
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	No dose adjustment is necessary in patients with mild or moderate renal or hepatic impairment; alirocumab has not been studied in severe renal or hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindication • Serious hypersensitivity reaction to the product Warnings • Allergic reactions
Special administration technique or considerations	• Administer as a subcutaneous injection into the thigh, abdomen, or upper arm; rotate injection sites. • The time to inject the medication may be longer than for other medications; up to 20 seconds with the use of the pen. • Allow the product to warm to room temperature for 30 to 40 minutes prior to use. • Do not administer the product if it has been at room temperature for 24 hours or longer. • If a dose is missed, advise the patient to administered the injection within 7 days of the missed dose, then resume the original schedule. If

	the missed dose is not given within 7 days, wait and administer the next dose on the original schedule.
Prepared by	Terri L. Levien, Pharm.D.

Daclatasvir / Daklinza / Bristol-Myers Squibb	
Generic Name / Brand Name / Company	Daclatasvir / Daklinza / Bristol-Myers Squibb
Date of approval	July 24, 2015
Drug Class (Mechanism of Action if novel agent)	Antiviral; hepatitis C virus NS5A inhibitor.
Indication	With sofosbuvir for the treatment with chronic hepatitis C virus genotype 3 infection.
Comparative agent – Therapeutic interchange?	Sofosbuvir + ribavirin; sofosbuvir + ribavirin + peginterferon alfa
Dosage forms/strengths. Common Dose/sig	Oral tablets: 30 mg & 60 mg Recommended dose: 60 mg once daily in combination with sofosbuvir for 12 weeks.
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	None identified
CLINICAL USE EVALUATION	
Common Adverse Effects	Headache, fatigue, nausea, diarrhea (≥5% incidence).
Severe Adverse Effects	Serious symptomatic bradycardia in patients taking amiodarone in combination with sofosbuvir and daclatasvir.
Severe Drug-Drug Interactions	Strong CYP3A4 inhibitors: may increase plasma levels of daclatasvir, reduce daclatasvir dose Moderate CYP3A4 inducers: increase daclatasvir dose Strong CYP3A4 inducers: may decrease plasma levels and thus reduce the therapeutic effects - contraindicated.
Severe Drug-Food Interactions	None, however if taken with high fat, high caloric meals, Cmax and AUC are decrease by 28% and 23% respectively.
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Lipase levels may increase to >3 times the upper limit of normal.
Used in Pediatric Areas	Safety and efficacy have not been studied in patients <18 years of age.
Renal or Hepatic Dosing	No dosage adjustment of daclatasvir is required for patient with any degree of renal impairment. No dosage adjustment of daclatasvir is required for patients with Child-Pugh A,B, or C. However safety and efficacy have not been studied in patients with decompensated cirrhosis nor for liver transplant patients.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindication • Combination with drugs that strongly induce CYP3A4, leading to lower exposure and loss of efficacy of daclatasvir. Warnings • Serious symptomatic bradycardia when coadministered with sofosbuvir and amiodarone.
Special administration technique or considerations	May be taken with or without food.
Prepared by	Kalvin Stoker, WSU PharmD candidate, 2016

Sonidegib / Odomzo / Novartis	
Generic Name / Brand Name / Company	Sonidegib / Odomzo / Novartis
Date of approval	July 24, 2015
Drug Class (Mechanism of Action if novel agent)	Hedgehog pathway inhibitor

Indication	For the treatment of adult patient with locally advanced basal cell carcinoma that has recurred following surgery or radiation therapy, or those patients who are not candidates for surgery or radiation therapy.
Comparative agent – Therapeutic interchange?	Vismodegib
Dosage forms/strengths. Common Dose/sig	Capsules: 200 mg Recommended daily dose is 200 mg once daily until disease progression or unacceptable toxicity.
DEA Schedule	Not applicable
Date of market availability	To be determined
Similar Medications (Look-Alike Sound-Alike)	None
CLINICAL USE EVALUATION	
Common Adverse Effects	Muscle spasms, alopecia, dysgeusia, fatigue, nausea, musculoskeletal pain, diarrhea, decreased appetite, decreased weight, myalgia, abdominal pain, headache, pain, vomiting, pruritus; increased serum creatinine, increased serum creatine kinase, hyperglycemia, increased lipase, increased ALT or AST, increased amylase, anemia, lymphopenia.
Severe Adverse Effects	Muscle spasms, musculoskeletal pain, fatigue, decreased weight
Severe Drug-Drug Interactions	Strong CYP3A4 inhibitors: cause increased sonidegib - avoid. Moderate CYP3A4 inhibitors: avoid long-term use Strong or moderate CYP3A4 inducers: result in decreased serum sonidegib - avoid
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 creatine kinase and creatinine prior to initiating, periodically during treatment, and as clinically indicated
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	No dosage adjustment is recommended for renal impairment. No adjustment recommended for patients with mild hepatic impairment. Sonidegib has not been studied in patients with moderate to severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Warnings • Associated with embryo-fetal death and severe birth defects. Verify pregnancy status prior to initiating sonidegib. Advise females of reproductive potential to use effective contraception during treatment and for at least 20 months after the last dose; advise males of the risk of exposure through semen and to use condoms during treatment and for at least 8 months after the last dose. • Advise patients to NOT donate blood or blood products while taking sonidegib and for at least 20 months after the last dose of sonidegib due to risk of blood products being given to females of reproductive potential. • Musculoskeletal adverse reactions, which may be accompanied by serum creatine kinase elevations, occur with sonidegib and other drugs which inhibit the hedgehog pathway. Interrupt sonidegib for severe or intolerable musculoskeletal adverse reactions. Permanently discontinue for serum CK greater than 2.5 times ULN with worsening renal function; serum CK elevation greater than 10 times ULN; recurrent serum CK elevation greater than 5 times ULN; recurrent severe or intolerable musculoskeletal adverse reactions.
Special administration technique or considerations	Take on an empty stomach.
Prepared by	Kalvin Stoker, WSU PharmD candidate, 2016