Highlights of FDA Activities – 11/1/15 – 11/30/15

FDA Drug Safety Communications & Drug Information Updates:

FDA Review Finds Long-term Treatment with Clopidogrel (Plavix) Does Not Change Risk of Death 11/06/15

In an update from an FDA Drug Safety Communication from November 16, 2014, the FDA has determined that long-term use of clopidogrel does not increase or decrease overall risk of death in patients with, or at risk for, heart disease. Additionally, the FDA review evaluated data from a number of trials and concluded that clopidogrel does not increase the risk of cancer or death from cancer. Overall, their reviews found no evidence of either a harm or benefit of clopidogrel on mortality in the select patient population with (or at risk for) coronary artery disease.

FDA Advises of Rare Cases of Underactive Thyroid in Infants Given Iodine-Containing Contrast Agents for Medical Imaging 11/17/15

The FDA is advising that rare cases of underactive thyroid have been reported in infants following use of contrast media containing iodine for medical imaging procedures. In all reported cases, infants were either premature or had other serious underlying medical conditions. Available evidence suggests this is rare and is usually temporary, resolving without treatment and without any lasting effects. Changes to labeling of all iodinated contrast media products have been approved by the FDA to include information about these cases.

Major Medication Recalls Announced Through MedWatch:

Compounded Multivitamins by Glades Drugs: Nationwide Recall due to High Amounts of Vitamin D3 (Cholecalciferol) 11/30/2015

The FDA announced an alert intended for both health care professionals and patients regarding a voluntary recall of compounded multivitamin capsules containing high amounts of Vitamin D3 (cholecalciferol) from Glades Drugs in Pahokee, Florida. The FDA has received several reports of adverse events associated with Vitamin D toxicity that may be linked to the use of these capsules.

Dietary Supplement Recalls & Public Notifications

In November 2015, 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)*
Power Khan	Sexual enhancement	Sildenafil, thiosildenafil
Rhino X	Sexual enhancement	Sildenafil
Australia Kangaroo Essence	Sexual enhancement	Sildenafil
Effective Viagra Tablets	Sexual enhancement	Sildenafil
Sex Drive Capsules	Sexual enhancement	Sildenafil
XForMan Plus	Sexual enhancement	Sildenafil
Perfect Slim Fast Track Slim	Weight loss	Fluoxetine, orlistat
Super Herbs	Weight loss	Sibutramine, desmethylsibutramine
Slyn Both	Weight loss	Fluoxetine, orlistat
Zero Fat	Weight loss	Sibutramine, fluoxetine
SPCARET Princess Diet	Weight loss	Sibutramine
Ultimate Herbal Slimcaps*	Weight loss	Sibutramine
Natureal*	Weight loss	Sibutramine

*Recalled

New Product Shortages Reported by the FDA:	***Date Initially Posted***
Sumatriptan (Imitrex, GSK) Nasal Spray – supply not available until February 2016	11/20/15

Product Discontinuations/Withdrawals	***Date Posted***
Oprelvekin (Neumega, Pfizer) lyophilized powder for injection Discontinued for business reasons; no other sources available.	11/10/15
Clonidine Hydrochloride and Chlorthalidone Tablets, USP (Clopres, Mylan Pharmaceuticals, Inc.) Discontinued for business reasons; no other sources available.	11/17/15
Quinapril Hydrochloride and Hydrochlorothiazide Tablets (Mylan Pharmaceuticals, Inc.) Discontinued for business reasons; other sources are available.	11/17/15
Clemastine fumarate 1.34 mg and 2.68 mg tablets (Sandoz) Discontinued for business reasons; other sources are available.	11/23/15

New Drug Approvals:	***Description***	***Date Approved***
Mepolizumab / Nucala / GlaxoSmithKline LLC	See attached drug summary	11/04/15
Elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide / Genvoya / Gilead Sciences Inc.	See attached drug summary	11/05/15
Cobimetinib / Cotellic / Genentech, Inc.	See attached drug summary	11/10/15
Osimertinib / Tagrisso / AstraZeneca Pharmaceuticals LP	See attached drug summary	11/13/15
Daratumumab / Darzalex / Janssen Biotech, Inc.	See attached drug summary	11/16/15
Ixazomib / Ninlaro / Millennium Pharmaceuticals, Inc.	See attached drug summary	11/20/15
Necitumumab / Portrazza / Eli Lilly and Company	See attached drug summary	11/24/15
Elotuzumab / Empliciti / Bristol-Myers Squibb	See attached drug summary	11/30/15

New Indications:	***Description***	***Date Approved***
Ledipasvir-sofosbuvir / Harvoni / Gilead	Indication expanded to include treatment of genotypes 4, 5 and 6 chronic hepatitis C virus infection, and treatment of patients with chronic hepatitis C infection who are co-infected with HIV-1	11/12/15
Ibuprofen injeciton / Caldolor Cumberland Pharmaceuticals	Indication expanded to include use in pediatric patients 6 months and older	11/20/15
Nivolumab / Opdivo / Bristol-Myers Squibb	Indication expanded to include patients with advanced (metastatic) renal cell carcinoma	11/23/15
Dabigatran / Pradaxa / Boehringer Ingelheim Pharmaceuticals	Indication expanded to include prophylaxis of deep vein thrombosis and pulmonary embolism in patients who have undergone hip replacement surgery; new 110 mg capsule strength	11/20/15
Anthrax vaccine adsorbed / BioThrax / Emergent BioDefense Operations	Indication expanded to include prevention of anthrax following suspected or confirmed exposure to Bacillus anthracis in adults 18 through 65 years of age	11/23/15

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Halobetasol propionate lotion / Ultravate / Ferndale Laboratories, Inc.	Lotion dosage form intended for use in the topical treatment of plaque psoriasis in patients 18 years and older.	11/06/15
Antihemophilic factor (Recombinant) PEGylated / Adynovate / Baxalta US Inc.	Approved for the as-needed treatment and control of bleeding episodes and prophylaxis of bleeding in patients 12 years and older with Hemophilia A. The modifications	11/13/15

	in this formulation are intended to potentially require less frequent injections than unmodified Antihemophilic Factor.	
Naloxone hydrochloride nasal spray / Narcan / Adapt Pharma, Inc.	The first FDA-approved nasal spray version of naloxone hydrochloride, a medication intended for intervention in an opioid overdose.	11/18/15
Esomeprazole magnesium delayed release tablet / Nexium 24H / AstraZeneca LP	Extended release oral tablet formulation of esomeprazole magnesium; joins the delayed release capsule formulation on the over-the-counter market.	11/23/15
Influenza vaccine, adjuvanted / Fluad / Novartis	Formulated with adjuvant MF59, an oil-in-water emulsion of squalene oil, to enhance the immune response of the vaccinated individual. Approved for use as a single IM injection in persons 65 years and older.	11/24/15

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Mepolizumab / Nucala / GlaxoSmithKline LLC	
Generic Name / Brand Name / Company	Mepolizumab / Nucala / GlaxoSmithKline LLC
Date of approval	11/04/15
Drug Class (Mechanism of Action if novel agent)	Interleukin-5 antagonist. Mepolizumab binds IL-5, inhibiting the bioactivity of IL-5 by blocking binding to eosinophils. Reduction of IL-5 signaling results in decreased survival and production of eosinophils, though the mechanism of mepolizumab in asthma is not definitively established.
Indication	Add-on maintenance treatment of severe asthma in patients ≥ 12 years old with an eosinophilic phenotype
Comparative agent – Therapeutic interchange?	None; indication overlaps with omalizumab, but mechanism differs
Dosage forms/strengths. Common Dose/sig	Injection: 100 mg lyophilized powder in a single-dose vial for reconstitution. Inject 100 mg subcutaneously every 4 weeks.
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Mepivacaine, meprobamate
CLINICAL USE EVALUATION	
Common Adverse Effects	Headache, injection site reaction, back pain, fatigue
Severe Adverse Effects	Hypersensitivity reactions, herpes zoster
Severe Drug-Drug Interactions	No formal drug interaction studies have been performed
Severe Drug-Food Interactions	None known
Important Lab Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Eosinophils
Used in Pediatric Areas	Safety and efficacy in pediatric patients younger than 12 years have not been established. 28 adolescents between the ages of 12 and 17 years old were enrolled in phase 3 studies, from which subjects had a reduction in rate of exacerbations that trended to favor mepolizumab. The adverse event profile was found to be generally similar to the overall population; although the mean apparent clearance was 35% less than that of adults.

Renal or Hepatic Dosing	No clinical trials were conducted to assess the effect of renal or hepatic impairment on dosing regimens. Mepolizumab is not renally cleared and is degraded by widely distributed proteolytic enzymes not restricted to hepatic tissue.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindicated in patients who have hypersensitivity to mepolizumab or excipients in the formulation. • Not for use in acute bronchospasm or status asthmaticus. • Herpes zoster infections have occurred in patients receiving mepolizumab. Consider varicella vaccination when appropriate. • Do not abruptly discontinue systemic or inhaled corticosteroids. • Treat patients with pre-existing helminth infections before starting mepolizumab therapy.
Special administration technique or considerations	• Should be reconstituted and administered by a healthcare professional. • Administer by subcutaneous injection into the upper arm, thigh, or abdomen.
Prepared by	Matthew Iguchi, Pharm.D. Candidate 2016

Elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide / Genvoya / Gilead Sciences Inc.	
Generic Name / Brand Name / Company	Elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide / Genvoya / Gilead Sciences Inc.
Date of approval	11/05/15
Drug Class (Mechanism of Action if novel agent)	Genvoya is a fixed-dose combination of antiretroviral drugs elvitegravir (boosted by CYP3A inhibitor cobicistat), emtricitabine, and tenofovir alafenamide.
Indication	Indicated as a complete regimen for the treatment of HIV-1 in adults and pediatric patients aged 12 years and older who have no antiretroviral treatment history or to replace current antiretroviral therapy in those who are virologically-suppressed on a stable antiretroviral regimen for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Genvoya.
Comparative agent – Therapeutic interchange?	Elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate (Stribild)
Dosage forms/strengths. Common Dose/sig	Tablets: 150 mg elvitegravir, 150 mg cobicistat, 200 mg emtricitabine, and 10 mg of tenofovir alafenamide Recommended Dose: One tablet daily with food.
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Gianvi
CLINICAL USE EVALUATION	
Common Adverse Effects	Diarrhea, nausea, fatigue, headache
Severe Adverse Effects	• Lactic acidosis/severe hepatomegaly with steatosis • Severe acute exacerbations of hepatitis B • Immune reconstitution syndrome • New onset or worsening renal impairment • Bone loss and mineralization defects
Severe Drug-Drug Interactions	Medications dependent on CYP3A4 are contraindicated with Genvoya: Alfuzosin, carbamazepine, phenobarbital, phenytoin, rifampin, dihydroergotamine, ergotamine, methylergonovine, cisapride, St. John's wort, lovastatin, simvastatin, pimozide, sildenafil (when dosed for pulmonary arterial hypertension), triazolam, and midazolam (oral) Medications that alter Genvoya concentrations:

	Acid reducing agents, antiarrhythmics, antibacterials, anticoagulants, antidepressants, antifungals, anti-gout, antimycobacterials, benzodiazepines, beta-blockers, calcium-channel blockers, systemic corticosteroid, inhaled/nasal corticosteroid, endothelin receptor antagonists, HMG-CoA reductase inhibitors, hormonal contraceptives, immunosuppressants, narcotic analgesics, inhaled beta agonists, neuroleptics, PDE5 inhibitors, and sedative hypnotics (see table in package insert).
Severe Drug-Food Interactions	None listed.
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Prior to initiation – hepatitis B virus, creatinine clearance, urine glucose, urine protein; during therapy monitor creatinine clearance, urine glucose, urine protein.
Used in Pediatric Areas	Approved for use in patients 12 years and older
Renal or Hepatic Dosing	No dosage adjustment in mild or moderate hepatic impairment; not recommended in patients with severe hepatic impairment (Child-Pugh Class C). No dosage adjustment in patients with CrCl greater than 30 mL/minute; not recommended in patients with a CrCl <30 mL/min because data in this population is insufficient.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Lactic acidosis/severe hepatomegaly with steatosis – reported with the use of nucleoside analogs in combination with other antiretrovirals • Patients coinfected with HIV-1 and HBV – Genvoya is not approved for the treatment of chronic HBV infection and safety and efficacy has not yet been established in patients coinfected with HIV-1 and HBV. • Avoid use with other antiretroviral products • Risk of adverse reactions or loss of virologic response due to drug interactions • Fat redistribution • Immune reconstitution syndrome • New onset or worsening renal impairment • Bone loss and mineralization defects
Special administration technique or considerations	• Take with food • Take medications containing aluminum and magnesium hydroxide or calcium carbonate at least 2 hours before or after taking Genvoya
Prepared by	Stephanie N. Lind and Matthew Iguchi, Pharm.D. Candidate 2016

Cobimetinib / Cotellic / Genentech Inc	
Generic Name / Brand Name / Company	Cobimetinib / Cotellic / Genentech Inc
Date of approval	11/10/15
Drug Class (Mechanism of Action if novel agent)	Cobimetinib is a reversible inhibitor of mitogen-activated protein kinase/extracellular signal regulated kinase 1 (MEK1) and MEK2
Indication	Treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation in combination with vemurafenib.
Comparative agent – Therapeutic interchange?	trametinib (Mekinist)
Dosage forms/strengths. Common Dose/sig	Tablets: 20 mg Recommended dose: 60 mg orally once daily for first 21 days of each 28-day cycle until disease progression or unacceptable toxicity.
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	None

CLINICAL USE EVALUATION	
Common Adverse Effects	Diarrhea, nausea, vomiting, sunburn/sun sensitivity, fever, increased GGT, increased CPK, hypophosphatemia, increased ALT, lymphopenia, increased AST, increased alkaline phosphatase, hyponatremia
Severe Adverse Effects	New primary malignancies (cutaneous and non-cutaneous), hemorrhage, cardiomyopathy, severe dermatologic reactions, serous retinopathy and retinal vein occlusion, hepatotoxicity, rhabdomyolysis, severe photosensitivity, embryo-fetal toxicity
Severe Drug-Drug Interactions	Avoid concomitant administration with strong or moderate CYP3A inducers or inhibitors.
Severe Drug-Food Interactions	None.
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Confirmation of BRAF V600E or V600K mutation in tumor specimens prior to initiation of therapy. Evaluate left ventricular ejection fraction (LVEF) prior to initiation, 1 month after initiation, and every 3 months thereafter until discontinuation of therapy Baseline liver function tests during treatment and as indicated Baseline creatine phosphokinase, 'periodically,' and as clinically indicated.
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	Safety and efficacy has not been studied in patients with moderate or severe hepatic impairment. Dose adjustment is not necessary for mild hepatic impairment. Dose adjustment is not necessary in patients with mild to moderate renal impairment. A recommended dose has not been established for patients with severe renal impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• New primary malignancies, cutaneous and non-cutaneous • Hemorrhage – monitor for bleeding • Cardiomyopathy – Grade 2 or 3 decrease in LVEF occurred in 26% of patients receiving cobimetinib with vemurafenib and 19% of patients receiving vemurafenib. Evaluate LVEF. • Severe dermatologic reactions – Grade 3 to 4 rash occurred in in 16% of patients receiving cobimetinib with vemurafenib. • Serous retinopathy and retinal vein occlusion – symptomatic and asymptomatic serous retinopathy was identified in 26% of patients receiving cobimetinib with vemurafenib. Onset of serous retinopathy events ranged from 2 days to 9 months and the duration ranged from 1 day to 15 months. Perform periodic ophthalmological evaluations. • Hepatotoxicity • Rhabdomyolysis – Grade 3 or 4 CPK elevations occurred in 12% of patients. • Severe photosensitivity – photosensitivity was reported in 47% of patients receiving cobimetinib with vemurafenib; advise patients to avoid sun exposure. • Embryo-fetal toxicity risk – use effective contraception
Special administration technique or considerations	Take with or without food. If a dose is missed, or vomiting occurs, take the next dose as scheduled
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Osimertinib / Tagrisso / AstraZeneca	
Generic Name / Brand Name / Company	Osimertinib / Tagrisso / AstraZeneca
Date of approval	11/13/15

Drug Class (Mechanism of Action if novel agent)	Kinase inhibitor
Indication	Indicated for patients with metastatic epidermal growth factor receptor T790M mutation-positive non-small cell lung cancer, as detected by a FDA-approved test, who have progressed on or after EGFR TKI therapy.
Comparative agent – Therapeutic interchange?	Cetuximab (Erbitux), lapatinib (Tykerb)
Dosage forms/strengths. Common Dose/sig	Tablets: 80 mg and 40 mg Dose: 80 mg by mouth once daily
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Tegaserod
CLINICAL USE EVALUATION	
Common Adverse Effects	Diarrhea, rash, dry skin, nail toxicity, nausea, decreased appetite, constipation, stomatitis, pruritus, cough, fatigue, back pain, headache, pneumonia, venous thromboembolism
Severe Adverse Effects	Interstitial lung disease/pneumonitis, QTc interval prolongation
Severe Drug-Drug Interactions	Avoid use with strong CYP3A inhibitors or inducers, or drugs that are sensitive substrates of CYP3A, breast cancer resistance protein (BCRP), or CYP1A2 with narrow therapeutic indices (e.g, fentanyl, cyclosporine).
Severe Drug-Food Interactions	May be dispersed in water; do not dissolve in any liquid except water.
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Comprehensive metabolic panel, platelet count
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients
Renal or Hepatic Dosing	No dosage adjustment is required in patients with mild or moderate renal impairment; there is no recommended dose for patients with severe renal impairment or end-stage renal disease. No dose adjustment is recommended in patients with mild hepatic impairment; there is no recommended dose for patients with moderate or severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Interstitial lung disease/pneumonitis – investigate if patient develops dyspnea, cough, and fever • QTc interval prolongation • Cardiomyopathy – evaluate LVEF before initiation and every 3 months • Embryo-fetal toxicity – use effective contraception
Special administration technique or considerations	Take with or without food. If the patient cannot swallow tablets whole, the patient may dissolve the tablet in 2 ounces of water until completely dissolved and drink right away. Add 4-8 more ounces of water to container and drink to ensure that the full dose is administered.
Prepared by	Stephanie N. Lind, PharmD Candidate 2016

Daratumumab / Darzalex / Janssen Biotech, Inc.	
Generic Name / Brand Name / Company	Daratumumab / Darzalex / Janssen Biotech, Inc.
Date of approval	11/16/15
Drug Class (Mechanism of Action if novel agent)	Antineoplastic agent, anti-CD38 monoclonal antibody
Indication	For patients with multiple myeloma who have received at least 3 prior lines of therapy including proteasome inhibitor and an immunomodulatory agent or who are double-refractory to a proteasome inhibitor and an immunomodulatory agent.
Comparative agent – Therapeutic interchange?	Nivolumab (Opdivo), rituximab (Rituxan)
Dosage forms/strengths. Common Dose/sig	Injection: 100 mg/5 mL solution in single-dose vial

	400 mg/5 mL solution in single-dose vial Recommended dose is 16 mg/kg body weight weekly during weeks 1 to 8, then every 2 weeks during weeks 9 to 24, and every 4 weeks from week 25 onwards until disease progression.
DEA Schedule	None.
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Dorzolamide, Durasal, Durezol
CLINICAL USE EVALUATION	
Common Adverse Effects	Infusion reactions, fatigue, nausea, back pain, pyrexia, cough, and upper respiratory tract infection.
Severe Adverse Effects	Infusion 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?)	None required.
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	No dose adjustments are necessary in renal impairment or mild hepatic impairment; has not been studied in moderate to severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Infusion reactions – approximately half or all patients studied experienced a reaction, most during the first infusion. • Initiate antiviral prophylaxis to prevent herpes zoster reactivation within 1 week of starting therapy and continuing until 3 months after treatment. • Interference with cross-matching and red blood cell antibody screening – type and screen prior to initiating therapy
Special administration technique or considerations	• Administer pre-infusion and post-infusion medications Pre-infusion: IV corticosteroid (methylprednisolone 100 mg or equivalent), oral antipyretics (acetaminophen 600-1000 mg), and oral or intravenous antihistamine (diphenhydramine 25-50 mg or equivalent). Post-infusion: Oral corticosteroid (20 mg methylprednisolone or equivalent) on first and second day after all infusions • Administer only as an intravenous infusion after dilution • Infusion Rates: (Full infusion completed in 15 hours) First Infusion 50 mL/hour (volume 1000 mL) and increase 50 mL/hour every hour [max 200 mL/hour] Second Infusion 50 mL/hour (volume 500 mL) with same rate change and max rate. Subsequent Infusions 100 mL/hour (volume 500 mL) with same rate change and max rate.
Prepared by	Stephanie N. Lind and Matthew Iguchi, Pharm.D. Candidates 2016

Ixazomib / Ninlaro / Millennium Pharmaceuticals, Inc.	
Generic Name / Brand Name / Company	Ixazomib / Ninlaro / Millennium Pharmaceuticals, Inc.
Date of approval	11/20/15
Drug Class (Mechanism of Action if novel agent)	Proteasome inhibitor
Indication	In combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy.

Comparative agent – Therapeutic interchange?	Elotuzumab (Empliciti), carfilzomib (Kyprolis), bortezomib (Velcade), cobimetinib (Cotellic)
Dosage forms/strengths. Common Dose/sig	Capsules: 4 mg, 3 mg, and 2.3 mg Recommended dosing: 4 mg taken orally on days 1, 8, and 15 of a 28-day cycle (1 hour before or at least 2 hours after food)
DEA Schedule	None
Date of market availability	Expected mid-December 2015
Similar Medications (Look-Alike Sound-Alike)	None
CLINICAL USE EVALUATION	
Common Adverse Effects	Diarrhea, constipation, thrombocytopenia, peripheral neuropathy, nausea, peripheral edema, vomiting, back pain.
Severe Adverse Effects	Thrombocytopenia, gastrointestinal toxicities, peripheral neuropathy, peripheral edema, cutaneous reactions, hepatotoxicity
Severe Drug-Drug Interactions	Avoid use with CYP3A inducers
Severe Drug-Food Interactions	Do not take with food. Take 1 hour before or at least 2 hours after food.
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Absolute neutrophil count, platelet count, liver enzymes
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	In moderate or severe hepatic impairment, reduce starting dose to 3 mg. In severe or end-stage renal disease requiring dialysis, reduce starting dose to 3 mg.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Thrombocytopenia – platelet nadirs typically occurring between days 14-21 of each 28-day cycle and recover to baseline by the next cycle • Gastrointestinal toxicities – adjust dose for severe diarrhea, constipation, nausea, or vomiting • Peripheral neuropathy – monitor and adjust dosing • Peripheral edema – monitor and adjust dosing • Cutaneous reactions – monitor and adjust dosing • Hepatotoxicity – monitor liver enzymes • Embryo-fetal toxicity – use effective contraception
Special administration technique or considerations	• Take in conjunction with lenalidomide and dexamethasone • Take 1 hour before or at least 2 hours after food • Take on the same day of the week for the first 3 weeks of each cycle, at about the same time of day • Do not take dexamethasone and ixazomib together • Swallow capsules whole and avoid direct contact with capsule contents.
Prepared by	Stephanie N. Lind & Matthew Iguchi, Pharm.D. Candidate 2016

Necitumumab / Portrazza / Eli Lilly and Company	
Generic Name / Brand Name / Company	Necitumumab / Portrazza / Eli Lilly and Company
Date of approval	11/24/15
Drug Class (Mechanism of Action if novel agent)	Epidermal growth factor receptor (EGFR) antagonist.
Indication	First-line treatment, in combination with gemcitabine and cisplatin, for patients with metastatic squamous non-small cell lung cancer.
Comparative agent – Therapeutic interchange?	Cetuximab (Erbitux), panitumumab (Vectibix)
Dosage forms/strengths. Common Dose/sig	Injection: 800 mg/50 mL solution in a single-dose vial Infuse 800 mg IV over 60 minutes on days 1 and 8 of each 3-week cycle.
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	None
CLINICAL USE EVALUATION	

Common Adverse Effects	Rash, hypomagnesemia, vomiting, diarrhea
Severe Adverse Effects	Cardiopulmonary arrest, venous and arterial thromboembolic events, infusion reactions, hypomagnesemia
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?)	Serum magnesium, calcium, and potassium prior to each infusion
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	No recommended dosing adjustments. No correlation between necitumumab exposure and renal/hepatic function were identified in clinical trials.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Increased toxicity and mortality in non-squamous non-small cell lung cancer • Electrolyte imbalances potentially leading to cardiopulmonary arrest – monitor serum electrolytes closely • Monitor for dermatologic toxicities – limit sun exposure • Monitor for infusion-related reactions – reduce infusion rate if necessary • Embryo-fetal toxicity – use effective contraception
Special administration technique or considerations	• Pre-medicate patients who have experienced a Grade 1 or 2 infusion-related reaction with diphenhydramine (or an equivalent) prior to all infusions; for patients who have experienced a second Grade 1 or 2 infusion-related reaction, pre-medicate with diphenhydramine, acetaminophen, and dexamethasone (or equivalents) prior to each infusion. • Reduce infusion rate by 50% for patients who have experienced an infusion-related reaction. • Stop infusion for all Grade 2 infusion-related reactions until the signs and symptoms have abated or decreased to Grade 1, at which point the infusion can be resumed at 50% for all subsequent infusions. • If a patient experiences Grade 3 or 4 infusion-related reaction, discontinue the medication immediately. Do no re-test. • Withhold for Grade 3 rash or acneiform rash until symptoms are at least at Grade 2 or better, at which point the dose should be reduced to 400 mg for at least one treatment cycle. If symptoms do not worse, the dose can be increased 200 mg each subsequent treatment cycle until the normal treatment dose of 800 mg is reached. • Discontinue if Grade 3 rash or acneiform rash persist at higher than Grade 2 for over 6 weeks, if reactions worsen/become intolerable at the reduced dose (400 mg), Grade 3 skin induration/fibrosis, or Grade 4 dermatologic toxicity. • Infusion should be given via infusion pump over 60 minutes through a separate infusion line; line should be flushed with 0.9% Sodium Chloride solution at end of infusion.
Prepared by	Matthew Iguchi, Pharm.D. Candidate 2016

Elotuzumab / Empliciti / Bristol-Myers Squibb Company	
Generic Name / Brand Name / Company	Elotuzumab / Empliciti / Bristol-Myers Squibb Company
Date of approval	11/30/15
Drug Class (Mechanism of Action if novel agent)	SLAMF7-directed immunostimulatory antibody

Indication	In combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.
Comparative agent – Therapeutic interchange?	ixazomib (Ninlaro), carfilzomib (Kyprolis), bortezomib (Velcade), cobimetinib (Cotellic)
Dosage forms/strengths. Common Dose/sig	Injection: 300 mg or 400 mg lyophilized powder in single-dose vial for reconstitution With lenalidomide and dexamethasone: 10 mg/kg administered every week for the first two 28-day cycles and every 2 weeks thereafter until disease progression or unacceptable toxicity.
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	None
CLINICAL USE EVALUATION	
Common Adverse Effects	Fatigue, diarrhea, pyrexia, constipation, cough, peripheral neuropathy, nasopharyngitis, upper respiratory tract infection, decreased appetite, pneumonia
Severe Adverse Effects	Infusion reactions, infections, second primary malignancies, hepatotoxicity
Severe Drug-Drug Interactions	No formal drug-drug interaction studies have been conducted.
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?)	Liver function tests
Used in Pediatric Areas	Safety and efficacy have not yet been established in pediatric patients.
Renal or Hepatic Dosing	None listed.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Infusion reactions – premedicate; interrupt for Grade 2 or higher • Infections – monitor for fever and other signs of infection • Second primary malignancies • Hepatotoxicity – monitor liver function • Interference with determination of complete response – elotuzumab can be detected on assays used for the clinical monitoring of endogenous M-protein, which can impact determination of response.
Special administration technique or considerations	• Premedicate with dexamethasone, diphenhydramine, ranitidine, and acetaminophen • Initiate infusion at a rate of 0.5 mL per minute, increasing in a stepwise manner to 2 mL/minute after 60 minutes for the first dose, and after 30 minutes for the second dose. If tolerated, infusion can be administered at 2 mL/min for all subsequent doses and increased to a maximum of 5 mL/min after 4 cycles.
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