WASHINGTON STATE UNIVERSITY HEALTH SCIENCES

Drug Information Center
College of Pharmacy and Pharmaceutical Sciences

Highlights of FDA Activities – 8/1/18 – 8/31/18

FDA Drug Safety Communications & Drug Information Updates:

Azithromycin - Increased Risk of Cancer Relapse with Long-Term Use After Donor Stem Cell Transplant 8/3/18
The FDA warned that azithromycin should not be prescribed for long-term prophylaxis of bronchitis obliterans in patients who undergo donor stem cell transplant due to increased potential for cancer relapse and death. A clinical trial observed an increased rate of relapse in cancers affecting the blood and lymph nodes, including death, in patients receiving azithromycin prophylaxis. The manufacturer of the brand name product will be distributing a Dear Healthcare Provider letter on this safety issue. The FDA is reviewing additional data and will communicate the conclusions and recommendations when the review is complete.

FDA Launches New Medication Guide Database 8/8/18
The FDA announced the availability of a new Medication Guide Database to replace the previous website. The new database allows active ingredients and brand name searches, download capability to spreadsheets, faster database updates, and improved mobile device usability.

Updated Prescribing Information for Pembrolizumab (*Keytruda*) and Atezolizumab (*Tecentriq*) 8/16/18
The FDA updated the prescribing information for pembrolizumab and atezolizumab to require the use of an FDA-approved companion diagnostic test to determine PD-L1 levels in tumor tissues from patients with locally advanced or metastatic urothelial cancer who are cisplatin-ineligible. This change followed the recent approval of companion diagnostics to determine PDL1 expression. The Dako PD-L1 IHC 22C3 PharmDx Assay was approved to determine PDL1 expression by using a combined positive score (CPS) assessing PD-L1 staining in tumor and immune cells, as specified in the pembrolizumab labeling. The Ventana PD-L1 (SP142) Assay is a companion diagnostic for atezolizumab that determines PD L1 expression in immune cells.

FDA Approves First Generic Version of EpiPen and EpiPen Jr Auto-Injectors 8/16/18
Teva Pharmaceuticals gained FDA approval to market its generic AB-rated/therapeutically equivalent version of the EpiPen and EpiPen Jr epinephrine auto-injector in 0.3 mg and 0.15 mg.

FDA Extends Expiration Dates for EpiPen Auto-Injectors 8/16/18
The FDA extended the expiration dates of specific lots of 0.3 mg Mylan auto-injectors by 4 months beyond the labeled expiration date based on stability provided by Pfizer and reviewed by the FDA to help mitigate the current product shortage. Patients should be instructed to continue to store these products as labeled.

FDA Takes Action Against 21 Websites Marketing Unapproved Opioids: 8/28/18
The FDA issued warning letters to four online networks (CoinRX, MedInc.biz, PharmacyAffiliates.org, and PharmaMedics) operating a total of 21 websites illegally marketing unapproved and misbranded versions of opioid medications, including tramadol.

Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitors for Diabetes: Warning - Rare Occurrences of a Serious Infection of the Genital Area 8/29/18
The FDA warned that cases of necrotizing fasciitis of the perineum or Fournier's gangrene, a rare but serious infection of the genitals and area around the genitals, have been reported with the SGLT2 inhibitor class. The FDA is requiring a new warning about this risk be added to the prescribing information of all SGLT2 inhibitors and to the patient Medication Guide. To date the FDA has identified 12 cases of Fournier's gangrene in patients taking a SGLT2 inhibitor. The cases included 7 men and 5 women, all of whom were hospitalized and required surgery; one patient died. Infection occurred within several months of initiating SGLT2 inhibitor therapy. In comparison, only 6 cases of Fournier's gangrene (all in men) were identified in review of other antidiabetic drug classes over a period of more than 30 years.

Major Medication/Drug-Related Product Recalls Announced Through MedWatch:

Valsartan Recalls 2018

The FDA continued to provide updates on valsartan recalls related to products found to contain NDMA in the active pharmaceutical ingredient, NDMA as an environmental contaminant, and testing methods for manufacturers to detect and quantify NDMA. The FDA maintains an updated list of valsartan products under recall and a list of valsartan products not under recall on a web page dedicated to the recall.

CVS Health 12 Hour Sinus Relief Nasal Mist and All Product Quest Manufacturing LLC Nasal Products and Baby Oral Gels: Recall – Microbial Contamination 8/8/18 & 8/28/18

Product Quest Manufacturing recalled one lot number of CVS Health 12 Hour Sinus Relief Nasal Mist (Lot# 173089J) to the consumer level after *Pseudomonas aeruginosa* was found in the product. Subsequently Product Quest expanded the recall at the retail level to include all lots of nasal products and baby oral gels manufactured at the company's Florida facility. There is no known microbial contamination associated with the products included in the expanded recall. A complete list of the recalled products labeled under the Best Choice, CVS, Discount Drug Mart, Dollar General, Family Dollar, Finafta, Harmon, Humist, Meijer, Premier Value, Quality Choice, Rexall, Rhinall, Rite-Aid, TC, Thayers, Well at Walgreens, and Valeant labels can be found on the FDA website.

Porcine Thyroid Active Pharmaceutical Ingredient (API) – Inconsistent Quality 8/17/18

The FDA alerted API repackagers and distributors, finished manufacturers, and compounders that Sichuan Friendly Pharmaceutical Co. Limited, China recalled certain lots of porcine thyroid due to inconsistent quality of API. FDA testing confirmed inconsistent levels of the active ingredients – levothyroxine and liothyronine – and advised the API should not be used to manufacture or compound drug for patient use. Patients are advised not to use porcine thyroid products made by Westminster, which were manufactured from API from Sichuan Friendly. Westminster recalled all lots of levothyroixine and liothyronine (thyroid tablets) 15 mg, 30 mg, 60 mg, 90 mg, and 120 mg on 8/9/18. Sichuan Friendly was placed on import alert 66-40 on March 22, 2018 for CGMP deviations observed during inspections.

Hydrochlorothiazide tablets USP 12.5 mg by Accord Healthcare Inc.: Recall – Labeling Mix-up 8/27/18

Accord Healthcare Inc. recalled one lot number of hydrochlorothiazide tablets USP 12.5 mg (Lot PW05264 – 46632 Bottles, NDC 16729-182-01) at the consumer level after a 100-count bottle of hydrochlorothiazide 12.5 mg tablets USP was found to contain 100 spironolactone 25 mg tablets USP.

Children's Advil Suspension Bubble Gum Flavored 4 fl oz bottle by Pfizer Inc.: Recall – Unmatched Dosage Cup 8/27/18

Pfizer Consumer Healthcare recalled one lot of Children's Advil Suspension Bubble Gum Flavored 4 fluid ounce Bottle (lot R51129, NDC 0573-0207-30) due to customer complaints that the dosage cup is marked in teaspoons and the instruction on the label are in milliliters (mL).

Montelukast by Camber Pharmaceuticals: Recall – Incorrect Drug in Bottles 8/31/18

Camber Pharmaceuticals recalled one lot of montelukast sodium tablets (lot MON17384, exp. 12/31/19, NDC 31722-726-30) to the consumer level following determination that sealed bottles labeled as montelukast sodium 10 mg tablets 30-count contained 90 losartan potassium 50 mg tablets.

Dietary Supplement Recalls & Public Notifications

Notifications were issued regarding undeclared active ingredients or contaminants in the following products. Patients are advised not to purchase or use these products.

Product	***Promoted Use***	***Undeclared Ingredient(s) or Contaminants***
5K	Sexual enhancement	Sildenafil[1]
BodySlim Herbal	Weight loss	Sibutramine[2]
Blissful Remedies Red Maeng Da 100% Mitragyna Speciosa*	Pain relief; sedation	Salmonella
Blissful Remedies Red Maeng Da Liquid Kratom Mitragyna Speciosa*	Pain relief; sedation	Salmonella
Blissful Remedies 4 Hour Chill Slow Motion Blend*	Pain relief; sedation	Salmonella
Blissful Remedies Gold Series Ultra Enhanced Indo (100% Mitragyna Speciosa)*	Pain relief; sedation	Salmonella
Blissful Remedies Kratom+CBD, CBD infused Maeng Da*	Pain relief; sedation	Salmonella
Compulsin (Lot CO/030717B) homeopathic HelloLife/King Bio*	Nervous, repetitive thoughts and behavior	*Burkholderia cepacia*
Ding Ji Wei Ge	Sexual enhancement	Sildenafil[1]
Easy 2 Slim	Weight loss	Sibutramine[2]
Extenze Nutritional Supplement	Sexual enhancement	Sildenafil[1]
Extenze Plus	Sexual enhancement	Sildenafil[1]
King Bio aqueous-based products (Dr. King's: Natural Medicine, Aquaflora, Natural Pet Pharmaceuticals, SafeCareRx, Natural Veterinary, and Safecare) liquids, oral sprays, nasal gels, creams, and lotions* (complete list)	Multiple promoted uses	Microbial contamination
Neuroveen (Lot NV/030717D) homeopathic HelloLife/King Bio*	Nerve pain	*Staphylococcus saprophyticus* and *Burkholderia cepacia*
Nuvitra	Weight loss	Fluoxetine, sibutramine[2]
Panther Power Platinum 11000	Sexual enhancement	Sildenafil[1]
Powerful Red Vein Bali Premium Kratom powder and capsules*	Pain relief; sedation	Salmonella
PremierZen Gold 4000	Sexual enhancement	Sildenafil[1]
Respitrol (Lot RE/030717E) homeopathic HelloLife/King Bio*	Respiratory symptoms	Microbial contaminants
Slimming Capsule	Weight loss	Sibutramine[2], phenolphthalein[3]
Super Green Maeng Da Premium Kratom powder and capsules*	Pain relief; sedation	Salmonella
Thyroveev (Lot TVV/030717F) homeopathic HelloLife/King Bio*	Thyroid	Microbial contaminants
Weight Away Remedy homeopathic (Lot 111417LWL614) Living Well Remedies	Weight loss	Microbial contaminants
XXXPlosion Ultra	Sexual enhancement	Sildenafil[1]

*Recalled

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

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

[3]Phenolpthalein is genotoxic and potentially carcinogenic; discontinued in 1999[FDA]

Product Discontinuations/Withdrawals	***Date Posted***
Atorvastatin tablets (Teva): remains available from other generic manufacturers	8/2/18
Ketoprofen (Teva): remains available from other generic manufacturers	8/3/18
Trazadone (Apotex): remains available from other generic manufacturers	8/7/18
Prednisone acetate 1% ophthalmic suspension (*Omnipred*, Novartis): remains available from other manufacturers	8/22/18
Darifenacin hydrobromide extended-release tablets 90-count bottles (Teva): 7.5 mg and 15 mg tablets remain available in 30-count bottles	8/22/18
Olaparib (*Lynparza*, AstraZeneca) 50 mg capsules: olaparib (*Lynparza*) remains available as 150 mg tablets and 100 mg tablets	8/28/18
Perphenazine tablets (Sandoz): remains available from other generic manufacturers	8/31/18

New Product Shortages	***Date Initially Posted***
Valsartan	8/3/18
Methocarbamol	8/17/18
Scopolamine transdermal system	8/27/18
Methyldopa tablets	8/30/18

New Drug Approvals:	***Description (See Attached Drug Summaries)***	***Date Approved***
Mogamulizumab / Poteligeo / Kyowa Kirin	Treatment of patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy	8/8/18
Patisiran / Onpattro / Alnylam Pharmaceuticals	Treatment of patients with peripheral nerve disease (polyneuropathy) caused by hereditary transthyretin-mediated amyloidosis (hATTR)	8/10/18
Segesterone acetate and ethinyl estradiol vaginal system / Annovera / Population Council	Combined hormonal contraceptive for women of reproductive age	8/10/18
Tafenoquine / Arakoda / 60 Degrees Pharmaceuticals	Indicated for malaria prophylaxis in adults	8/10/18
Migalastat / Galafold / Amicus Therapeutics U.S.	Treatment of adult patients with Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on laboratory data.	8/10/18
Stiripentol / Diacomit / Biocodex	Treatment of seizures associated with Dravet syndrome in patients 2 years and older taking clobazam	8/21/18
Cenegermin / Oxervate / Dompé farmaceutici SpA	Treatment of neurotrophic keratitis, a rare disease affecting the cornea	8/22/18
Lanadelumab / Takhzyro / Shire Pharmaceutical	First monoclonal antibody for the treatment of types I and II hereditary angioedema in patients aged 12 years and older	8/23/18
Eravacycline / Xerava / Tetraphase Pharmaceuticals	Treatment of complicated intra-abdominal infections	8/27/18
Doravirine / Pifeltro / Merck Sharp Dohme	In combination with other antiretrovirals in the treatment of HIV-1 in antiretroviral treatment naïve adult patients	8/30/18
Antihemophilic factor (recombinant), PEGylated-aucl / JIVI / Bayer HealthCare	For use in previously treated adults and adolescents with hemophilia A (congenital Factor VIII deficiency)	8/30/18

New Indications:	***Description***	***Date Approved***
Lenvatinib / Lenvima / Eisai	First-line treatment of patients with unresectable hepatocellular carcinoma	8/15/18
Nivolumab / Opdivo / Bristol-Myers Squibb	Metastatic small cell lung cancer not responding to chemotherapy and one other drug	8/16/18
Pembrolizumab / Keytruda / Merck	In combination with pemetrexed and platinum chemotherapy as first line treatment of patients with metastatic, non-squamous non-small cell lung cancer, with no EGFR or ALK genomic tumor aberrations.	8/20/18
Ivacaftor / Kalydeco / Vertex	Indication expanded to include patients 12 months to younger than 2 years with cystic fibrosis who have at least one mutation responsive to ivacaftor	8/15/18

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Lumacaftor and ivacaftor granule / Orkambi / Vertex	Unit-dose packets of oral granules for use in patients 2 years and older, homozygous for the F508del-CFTR mutation in the CFTR gene	8/7/18
Methylphenidate hydrochloride extended release capsules / Jornay PM / Ironshore	Capsules to be taken only in the evening. Exhibits both delayed-release and extended-release properties	8/8/18
Doravirine; lamivudine; tenofovir disoproxil fumarate / Delstrigo / Merck Sharp Dohme	Complete regimen for treatment of HIV-1 in adult patients with no antiretroviral treatment history	8/30/18
Loteprednol etabonate ophthalmic suspension / Inveltys / Kala	Twice-daily eye drop for treatment of inflammation and pain following ocular surgery	8/22/18
Tretinoin lotion 0.05% / Altreno / Ortho Dermatologics	Lotion dosage form for the treatment of acne in patients 9 years of age and older	8/23/18
Cyclosporine 0.09% ophthalmic solution / Cequa / Sun Pharma	Treatment of dry eye	8/14/18
Buprenorphine 16 mg/naloxone 4mg / Cassipa/ Teva Pharmaceuticals Inc.	Maintenance treatment of opioid dependence	9/7/18

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New Drug Approvals

Mogamulizumab-KPKC / Poteligeo / Kyowa Kirin	
Generic Name / Brand Name / Company	Mogamulizumab-KPKC / Poteligeo / Kyowa Kirin
Date of approval	8/8/2018
Drug Class (Mechanism of Action if novel agent)	Anti-CC chemokine receptor 4 antibody MOA: IgG monoclonal antibody that binds to CCR4 which depletes target cells. CCR4 is expressed on the surface of some T-cell malignancies and is expressed on regulatory T-cells.
Indication	Treatment of adult patients with relapsed or refractory mycosis fungoides or Sezary syndrome after at least one prior systemic therapy.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Injection: 20 mg/5 mL single dose vial Dosage: 1 mg/kg administered as IV infusion over at least 60 minutes Administer on days 1, 8, 15, and 22 for first 28-day cycle, then on days 1 and 15 of each subsequent 28-day cycle until disease progression or unacceptable toxicity
DEA Schedule	Not applicable
Date of market availability	Fourth quarter 2018
Similar Medication Names	None
Clinical Use Evaluation	
Common Adverse Effects	≥ 20%: rash, infusion related reactions, fatigue, diarrhea, musculoskeletal pain, and upper respiratory tract infection
Severe Adverse Effects	Stevens-Johnson syndrome, toxic epidermal necrolysis, myositis, myocarditis, polymyositis, hepatitis, pneumonitis, new-onset hypothyroidism, sepsis, pneumonia, skin infections, acute-GVHD, steroid-refractory GVHD, transplant-related death
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.	Pregnancy testing for females of reproductive potential prior to initiation.
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	Renal: not studied with CrCl less than 50 mL/min Hepatic: not studied in hepatic transaminase greater than or equal to 2.5 times the upper limit of normal
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No known contraindications. Warnings: Temporarily interrupt infusion for moderate to severe skin rashes; for life threatening rash: permanently discontinue. Monitor for infections and treat promptly. Interrupt or permanently discontinue as appropriate for autoimmune complications. Monitor for severe acute graft-versus-host disease and steroid-refractory GVHD. Verity pregnancy status prior to initiating; advise females of reproductive potential to use effective contraception during therapy and for 3 months after.
Special administration technique or considerations	Administer through an IV line containing a sterile, low protein binding, 0.22 micron (or equivalent) in-line filter. Do not co-administer with other medications in the same IV line. Administer premedication with diphenhydramine and acetaminophen for the first infusion.
Prepared by	Zachary Diekmann & Brittany Craft
Source	Poteligeo (mogamulizumab-kpkc) [prescribing information]. Bedminster, NJ: Kyowa Kirin, Inc.; August 2018.

Patisiran / Onpattro / Ajinomoto Althea, Inc.	
Generic Name / Brand Name / Company	Patisiran / Onpattro / Ajinomoto Althea, Inc.
Date of approval	8/10/18
Drug Class (Mechanism of Action if novel agent)	Transthyretin-directed small interfering RNA MOA: interferes with RNA production of an abnormal form of the protein transthyretin (TTR), therefore reducing the accumulation of amyloid deposits in peripheral nerves.
Indication	Treatment of adult patients with peripheral nerve disease (polyneuropathy) caused by hereditary transthyretin-mediated amyloidosis (hATTR)
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Lipid complex injection: 10 mg/5 mL (2 mg/mL) Dosage (based on actual body weight): 0.3 mg/kg in patients weighing less than 100 kg, or 30 mg in patients weighing 100 kg or more, administered by IV infusion every 3 weeks
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medication Names	Patiromer
Clinical Use Evaluation	
Common Adverse Effects	≥ 10%: upper respiratory tract infections and infusion–related reactions
Severe Adverse Effects	Hypotension and syncope during infusion; atrioventricular heart block
Severe Drug-Drug Interactions	None known
Severe Drug-Food Interactions	None
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None
Used in Pediatric Areas	Safety and effectiveness not been established
Renal or Hepatic Dosing	No adjustments in mild hepatic impairment (bilirubin ≤1 x ULN and AST >1 x ULN, or bilirubin >1.0 to 1.5 x ULN); not studied with moderate or severe impairment No dose adjustments in mild or moderate renal impairment; not studied in severe impairment or end-stage renal disease
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No known contraindications. Warnings: Infusion-related reactions: Monitor for signs and symptoms of infusion-related reactions, slow or interrupt the infusion if clinically indicated. Discontinue the infusion if a serious or life-threatening reaction occurs. Reduced serum vitamin A levels: Supplement with the recommended daily allowance of vitamin A. If ocular symptoms occur, refer to ophthalmologist.
Special administration technique or considerations	Should be administered by a healthcare professional. Administer IV via ambulatory infusion pump with a 1.2 micron polyethersulfone in-line filter. Use infusion sets and lines that are DEHP-free. Infuse over approximately 80 minutes. All patients should receive premedication (IV corticosteroid, oral acetaminophen, IV H1 blocker, and IV H2 blocker) given on the day of infusion at least 60 minutes prior to the start of infusion.
Prepared by	Brittany Craft
Source	Onpattro (patisiran) [prescribing information]. San Diego, CA: Ajinomoto Althea, Inc.; August 2018

Tafenoquine / Arakoda / 60 Degrees Pharmaceuticals LLC.	
Generic Name / Brand Name / Company	Tafenoquine / Arakoda / 60 Degrees Pharmaceuticals LLC.
Date of approval	8/8/18
Drug Class (Mechanism of Action if novel agent)	Antimalarial aminoquinolone
Indication	Prophylaxis of malaria in patients aged 18 years and older
Comparative agent – Therapeutic interchange?	Mefloquine
Dosage forms/strengths. Common Dose/sig	Tablets: 100 mg. The recommended dose is 200 mg once daily for 3 days before date of travel as a loading dose, then 200 mg once weekly starting 7 days after the last loading dose while in the malarious area, then 200 mg one time 7 days after the last maintenance dose upon exit from malarious area
DEA Schedule	Not applicable
Date of market availability	Early 2019
Similar Medication Names	Doxycycline, mefloquine, primaquine, atovaquone-proguanil
Clinical Use Evaluation	
Common Adverse Effects	≥1%: headache, dizziness, back pain, diarrhea, nausea, vomiting, increased alanine aminotransferase, motion sickness, insomnia, depression, abnormal dreams, anxiety
Severe Adverse Effects	Hypersensitivity reaction, hallucinations, hemolytic anemia, methemoglobinemia
Severe Drug-Drug Interactions	Potential increase in OCT2 and MATE substrates (e.g. metformin, dofetilide); avoid co-administration
Severe Drug-Food Interactions	None
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Test for glucose-6-phosphate dehydrogenase (G6PD) deficiency prior to prescribing. Pregnancy testing is recommended prior to initiating tafenoquine in females of reproductive potential.
Used in Pediatric Areas	Safety and efficacy not established
Renal or Hepatic Dosing	Not studied; monitor for adverse effects if used in patients with renal or hepatic impairment
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: G6PD deficiency or unknown G6PD status, patients with a history of psychotic disorders or current psychotic symptoms, or known hypersensitivity to tafenoquine, 8-aminoquinolines, or any of the product ingredients. Also contraindicated in breastfeeding if the infant is G6PD deficiency or G5PD status unknown. Warnings: hemolytic anemia in patients with G6PD deficiency, methemoglobinemia, psychiatric effects, and hypersensitivity reactions. Avoid pregnancy or use effective contraception during treatment and for 3 months after the final dose. There is a potential for delayed adverse reactions due to the long half-life (approximately 17 days).
Special administration technique or considerations	Administer with food. Swallow tablet whole. Complete the full course including the loading dose and the terminal dose.
Prepared by	Zach Diekmann
Source	Arakoda (tafenoquine) [prescribing information]. Washington DC. Sixty Degrees Pharmaceuticals, LLC. 2018.

Migalastat / Galafold / Amicus Therapeutics, Inc.	
Generic Name / Brand Name / Company	Migalastat / Galafold / Amicus Therapeutics, Inc.
Date of approval	8/10/18
Drug Class (Mechanism of Action if novel agent)	Alpha-galactosidase A pharmacological chaperone MOA: reversibly binds to the active site of the alpha-galactosidase A (alpha-Gal A) protein (encoded by the galactosidase alpha gene, GLA) that is deficient in Fabry disease. This binding stabilizes alpha-Gal A to allow its trafficking from the endoplasmic reticulum into the lysosome where it exerts its action.
Indication	Treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene variant based on in vitro assay data.
Comparative agent – Therapeutic interchange?	Agalsidase beta
Dosage forms/strengths. Common Dose/sig	Capsules: 123 mg. The recommended dose is 123 mg orally once every other day at the same time of day.
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medication Names	Miglustat
Clinical Use Evaluation	
Common Adverse Effects	≥ 10%: headache, nasopharyngitis, urinary tract infection, nausea, and pyrexia
Severe Adverse Effects	None
Severe Drug-Drug Interactions	None
Severe Drug-Food Interactions	Administration one hour before a high-fat or light meal or one hour after a light meal reduced AUC by 37% to 42% and Cmax by 15% to 39% compared to the fasting state
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Confirmed Fabry disease with an amenable GLA variant.
Used in Pediatric Areas	Safety and effectiveness have not been established
Renal or Hepatic Dosing	No dose adjustment in mild to moderate renal impairment. Not recommended in severe renal impairment or end-stage renal disease requiring dialysis. Not studied in eGFR less than 30 mL/min/1.73m^2. No dose adjustment in hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No known contraindications. Warnings: None known
Special administration technique or considerations	Do not eat at least 2 hours before and 2 hours after taking migalastat; only clear liquids allowed. Do not take on 2 consecutive days. Swallow capsules whole.
Prepared by	Brittany Craft
Source	Galafold (migalastat) [prescribing information]. Cranbury, NJ: Amicus Therapeutics U.S. Inc.; August 2018

Segesterone acetate and ethinyl estradiol vaginal system / Annovera / Population Council	
Generic Name / Brand Name / Company	Segesterone acetate and ethinyl estradiol vaginal system / Annovera / Population Council
Date of approval	8/10/18
Drug Class (Mechanism of Action if novel agent)	Combined hormonal contraceptive
Indication	For females of reproductive potential to prevent pregnancy
Comparative agent – Therapeutic interchange?	Etonogestrel/ethinyl estradiol vaginal ring (NuvaRing)
Dosage forms/strengths. Common Dose/sig	Vaginal system containing 103 mg segesterone acetate and 17.4 mg ethinyl estradiol. The vaginal system must remain in place continuously for 3 weeks (21 days) followed by a 1-week (7-day) vaginal system-free interval. One vaginal system provides contraception for thirteen 28-day cycles (1 year).
DEA Schedule	None
Date of market availability	Anticipated for fourth quarter of 2019 or first quarter of 2020
Similar Medication Names	
Clinical Use Evaluation	
Common Adverse Effects	>5%: headache/migraine, nausea/vomiting, vaginal infection/candidiasis, abdominal pain, dysmenorrhea, vaginal discharge, UTI, breast tenderness/pain/discomfort, metrorrhagia, diarrhea, genital pruritus
Severe Adverse Effects	Venous thrombolic events, psychiatric events, drug hypersensitivity reactions, spontaneous abortions
Severe Drug-Drug Interactions	Concomitant use with metabolic enzyme inducers (eg, CYP3A4) may decrease effectiveness or increase breakthrough bleeding. Vaginal products containing oil or silicone increase hormone exposure and should not be used.
Severe Drug-Food Interactions	Grapefruit juice may increase systemic exposure
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None required
Used in Pediatric Areas	Safety and efficacy is expected to be the same for postpubertal adolescents under the age of 18 as for those 18 and older
Renal or Hepatic Dosing	No studies have been conducted on renal or hepatic impairment. Acute or chronic disturbance of liver function may necessitate discontinuation until markers of liver function return to normal. It is not recommended in patients with renal impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in females with high risk of arterial or venous thrombotic diseases, current or history of breast cancer or other estrogen- or progestin-sensitive cancers, liver tumors, acute hepatitis, or severe cirrhosis, undiagnosed abnormal uterine bleeding, hypersensitivity to any of the product components, or use of Hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir. Cautions are the same as other combined hormonal contraceptives. A back-up method of contraception should be used if the system is out for more than 2 hours cumulative during the 21 days of continuous use.
Special administration technique or considerations	The same ring system is used for thirteen 28 day cycles or one year. The vaginal system should be stored in the case provided for the week it is out. Wash with mild soap and warm water, rinse, and pat dry with clean cloth towel before storage.
Prepared by	Zach Diekmann
Source	Annovera (segesterone acetate and ethinyl estradiol) [prescribing information]. New York, NY. Population Counsel. 2018.

Stiripentol / Diacomit / Biocodex	
Generic Name / Brand Name / Company	Stiripentol / Diacomit / Biocodex
Date of approval	8/21/18
Drug Class (Mechanism of Action if novel agent)	Anticonvulsant; Mechanism of anticonvulsant effect in humans is unknown. Possible mechanisms of action include direct effects mediated through the $GABA_A$ receptor and indirect effects involving inhibition of CYP450 activity with resulting increase in blood levels of clobazam and its active metabolite.
Indication	Treatment of seizures associated with Dravet syndrome in patients 2 years and older taking clobazam
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Capsule: 250 mg or 500 mg Powder for Oral Suspension: 250 mg or 500 mg The recommended dose is take 50 mg/kg/day divided in 2 or 3 divided doses (i.e. 16.67 mg/kg three times daily or 25 mg/kg twice daily). If the exact dose is not achievable given the available strengths, round to the nearest possible dose, which is usually within 50 mg to 150 mg of the recommended 50 mg/kg/day. The maximum recommended dose is 3,000 mg/day.
DEA Schedule	Not applicable
Date of market availability	Unknown
Similar Medication Names	None
Clinical Use Evaluation	
Common Adverse Effects	>10%: somnolence, decreased appetite, agitation, ataxia, weight decreased, hypotonia, nausea, tremor, dysarthria, insomnia
Severe Adverse Effects	Suicidal behavior and ideation, neutropenia, thrombocytopenia
Severe Drug-Drug Interactions	Stiripentol may increase clobazam concentrations; consider clobazam dose reduction if adverse effects occur. CYP2C8, CYP2C19, P-gp, and BCRP substrates may require dose reduction. CYP1A2, CYP2B6, and CYP3A4 substrates may require dose adjustment. CYP1A2, CYP3A4, and CYP2C19 inducers may necessitate stiripentol dose increase.
Severe Drug-Food Interactions	None
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Hematologic testing prior to starting treatment and every 6 months
Used in Pediatric Areas	Use in patients 2 to 18 years of age has been established.
Renal or Hepatic Dosing	Use is not recommended in moderate or severe renal impairment or moderate or severe hepatic impairment
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No known contraindications. Monitor weight and growth rate of pediatric patients. Assess for somnolence with other CNS depressants, if occurs, consider reduction of clobazam by 25%. Discontinue gradually to minimize risk of increased seizure frequency and status epilepticus
Special administration technique or considerations	Capsules must be swallowed whole with a glass of water during a meal. Powder for Oral Suspension should be mixed in a glass of water and should be taken immediately after mixing during a meal. Mix packet of oral powder into a small drinking cup with 100 mL of water. Powder for suspension contains phenylalanine.
Prepared by	Brittany Craft
Source	Diacomit (stiripentol) [prescribing information]. Beauvais, France: Biocodex; August 2018.

Lanadelumab-flyo / Takhzyro / Shire	
Generic Name / Brand Name / Company	Lanadelumab-flyo / Takhzyro / Shire
Date of approval	8/23/18
Drug Class (Mechanism of Action if novel agent)	Plasma kallikrein inhibitor; human IgG1 monoclonal antibody
Indication	Prophylaxis to prevent attacks of hereditary angioedema in patients 12 years and older
Comparative agent – Therapeutic interchange?	C1 inhibitor
Dosage forms/strengths. Common Dose/sig	Injection: 300 mg/2 mL solution in a single dose vial. Administer 300 mg every 2 weeks. Dosing every 4 weeks may be considered in some patients
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	None identified
CLINICAL USE EVALUATION	
Common Adverse Effects	>10%: Injection site reaction, upper respiratory infection, headache, rash, myalgia, dizziness, diarrhea
Severe Adverse Effects	Hypersensitivity
Severe Drug-Drug Interactions	No dedicated 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?)	None required
Used in Pediatric Areas	Safety and efficacy not established in patients less than 12 years of age
Renal or Hepatic Dosing	Not studied; no routine dosage adjustments recommended
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Discontinue administration in case of severe hypersensitivity reactions.
Special administration technique or considerations	Patients may self-administer. Vial should be taken out of the refrigerator 15 minutes before injecting to allow it to equilibrate to room temperature. Use an 18-gauge needle to draw up the solution and use a 27-gauge, ½ inch needle or other needle suitable for subcutaneous injection. Inject into the abdomen, thigh, or upper arm.
Prepared by	Zach Diekmann
Source	Takhzyro (lanadelumab-flyo) [prescribing information]. Lexington, MA: Dyax Corp.; August 2018.

Cenegermin-bkbj / Oxervate / Dompé farmaceutici S.p.A.	
Generic Name / Brand Name / Company	Cenegermin-bkbj / Oxervate / Dompé farmaceutici S.p.A.
Date of approval	8/22/2018
Drug Class (Mechanism of Action if novel agent)	Recombinant human nerve growth factor MOA: Nerve growth factor that is an endogenous protein involved in differentiation and maintenance of neurons and acts through specific high-affinity (i.e., TrKa) and low-affinity (i.e. p75NTR) nerve growth factor receptors in the anterior segment of the eye to support corneal innervation and integrity.
Indication	Treatment of neurotrophic keratitis
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Ophthalmic solution: 0.002% (20 mcg/mL) in a multiple-dose vial. Dosage: one drop in the affected eye(s) 6 times per day at 2-hour intervals, for eight weeks
DEA Schedule	Not applicable
Date of market availability	Early 2019
Similar Medication Names	None

Cenegermin-bkbj continued…	
Clinical Use Evaluation	
Common Adverse Effects	> 5%: eye pain, ocular hyperemia, eye inflammation and increased lacrimation
Severe Adverse Effects	None reported
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.	None
Used in Pediatric Areas	Safety and effectiveness established in patients 2 years and older
Renal or Hepatic Dosing	Not studied. No routine dosage adjustments recommended.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No labeled contraindications. Warnings: Remove contact lenses before applying and wait 15 minutes after instillation of the dose before reinserting contacts.
Special administration technique or considerations	Use cenegermin-bkbj first and wait at least 15 minutes before using other eye products. Product is stored in freezer at pharmacy. Patient should remove weekly carton from the insulated container and store for up to 14 days in a refrigerator (no later than 5 hours from when the medication is received from the pharmacy). If treatment is started immediately after receiving the carton, wait until the first vial is thawed (can take up to 30 minutes when kept at room temp). Do not shake the vial. Assemble the vial adapter to the vial (do not remove it). Wipe the surface of the valve on the connector part of the vial adapter. Remove pipette and screw onto the vial adapter. Turn vial upside down and draw the solution into the pipette. After filling the pipette, unscrew it from the vial adapter. Tilt head back and gently push the plunger down until at least 1 drop is released into the conjunctival fornix; blink a few times to cover the surface of the eye. Dispose of the used pipette.
Prepared by	Brittany Craft
Source	Oxervate (cenegermin-bkbj) [prescribing information]. Boston, MA: Dompe U.S. Inc.; August 2018.

Eravacycline / Xerava / Tetraphase Pharmaceuticals, Inc.	
Generic Name / Brand Name / Company	Eravacycline / Xerava / Tetraphase Pharmaceuticals, Inc.
Date of approval	8/27/18
Drug Class (Mechanism of Action if novel agent)	Tetracycline antibacterial
Indication	Complicated intra-abdominal infections in patients 18 years or older
Comparative agent – Therapeutic interchange?	Tigecycline (no head-to-head comparison)
Dosage forms/strengths. Common Dose/sig	Injection: 50 mg of eravacycline (equivalent to 63.5 mg eravacycline dihydrochloride) as a lyophilized powder in a single-dose vial for reconstitution and further dilution. Administer 1 mg/kg by IV infusion over approximately 60 minutes every 12 hours for 4-14 days; calculate dose using actual body weight
DEA Schedule	Not applicable
Date of market availability	Expected 4th quarter 2018
Similar Medication Names	Tetracycline

Eravacycline continued…	
Clinical Use Evaluation	
Common Adverse Effects	≥ 3%: infusion site reactions, nausea, and vomiting
Severe Adverse Effects	*Clostridium difficile*-associated diarrhea, tooth discoloration and enamel hypoplasia, inhibition of bone growth, hypersensitivity reactions
Severe Drug-Drug Interactions	Concomitant use of strong CYP3A inducers may reduce efficacy; increase the dose in patients taking strong CYP3A inducer. Concomitant use of anticoagulant therapy may require downward adjustment of the anticoagulant dose.
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None reported
Used in Pediatric Areas	Safety and effectiveness has not been established in pediatric patients. Due to adverse effects on tooth development and bone growth, not recommended in patients less than 8 years of age.
Renal or Hepatic Dosing	No adjustments warranted in renal impairment or mild to moderate hepatic impairment (Child Pugh A and B). Adjust dose in patients with severe hepatic impairment (Child Pugh C) to 1 mg/kg every 12 hrs on day 1, then 1 mg/kg every 24 hrs starting on day 2 for a total duration of 4 to 14 days.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in known hypersensitivity to eravacycline, tetracycline-class antibacterial drugs, or any of the excipients. Warnings: Avoid during tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) due to risk of permanent discoloration of teeth (yellow-gray-brown) and enamel hypoplasia. May cause reversible inhibition of bone growth when used during the second and third trimester of pregnancy, infancy, and up to 8 years of age. Evaluate for *Clostridium-difficile* if diarrhea occurs.
Special administration technique or considerations	Infused over approximately 60 minutes. May be administered through a dedicated line or through a Y-site. If the same line is used for sequential infusion, flush the line before and after with 0.9% sodium chloride injection.
Prepared by	Zach Diekmann and Brittany Craft
Source	Xerava (eravacycline) [prescribing information]. Watertown, MA: Tetraphase Pharmaceuticals, Inc; 2018.

Doravirine / Pifeltro / Merck & Co., Inc.	
Generic Name / Brand Name / Company	Doravirine / Pifeltro / Merck & Co., Inc.
Date of approval	8/30/18
Drug Class (Mechanism of Action if novel agent)	Non-nucleoside reverse transcriptase inhibitor (NNRTI)
Indication	Treatment of HIV-1 infection in adult patients with no prior antiretroviral treatment history in combination with other antiretroviral agents
Comparative agent – Therapeutic interchange?	Rilpivirine, Etravirine, Efavirenz
Dosage forms/strengths. Common Dose/sig	Tablets: 100 mg. Dose: one tablet orally once daily with or without food. Also available in combination dosage form (Delstrigo) containing doravirine 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg; administered as one tablet orally once daily with or without food.
DEA Schedule	None
Date of market availability	Unknown
Similar Medication Names	Darunavir, etravirine

Doravirine continued…	
Clinical Use Evaluation	
Common Adverse Effects	≥ 5%: nausea, dizziness, headache, fatigue, diarrhea, abdominal pain, and abnormal dreams
Severe Adverse Effects	Immune Reconstitution Syndrome
Severe Drug-Drug Interactions	Concomitant use of strong CYP3A inducers may reduce efficacy; avoid concomitant use or increase the doravirine dose in patients taking strong CYP3A inducer. Contraindicated with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, enzalutamide, rifampin, rifapentine, mitotane, and St. John's wort (Hypericum perforatum). Increase dose if coadministered with rifabutin. Co-administration with efavirenz, etravirine, or nevirapine is not recommended due to decrease in doravirine concentration.
Severe Drug-Food Interactions	None known.
Important Labs Values to assess prior to order entry or at point of clinical follow up.	HIV viral load and CD4+ cell counts
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	Renal: No adjustment in mild, moderate, or severe renal impairment. Not studied in end-stage renal disease or dialysis. Hepatic: No adjustment in mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Not studied in severe impairment (Child-Pugh C).
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindication: co-administration with strong CYP3A inducers Warnings: Monitor for Immune Reconstitution Syndrome during the initial phase of combination antiretroviral treatment; may develop an inflammatory response to indolent or residual opportunistic infections such as Mycobacterium avium infection, cytomegalovirus, Pneumocystis jirovecii pneumonia (PCP)
Special administration technique or considerations	Keep drug and desiccant in the original bottle, do not store in a pill box. Take the same time every day.
Prepared by	Zachery Diekmann and Brittany Craft
Source	Pifeltro (doravirine). [prescribing information]. Whitehouse Station, NJ: Merck & Co. Inc.; August 2018.

antihemophilic factor (recombinant), PEGylated-aucl / Jivi / Bayer HealthCare LLC	
Generic Name / Brand Name / Company	antihemophilic factor (recombinant), PEGylated-aucl / Jivi / Bayer HealthCare LLC
Date of approval	8/30/18
Drug Class (Mechanism of Action if novel agent)	Antihemophilic agent. Site-specific PEGylated recombinant antihemophilic factor that temporarily replaces the missing coagulation Factor VIII
Indication	For use in previously treated adults and adolescents (12 years of age or older) with hemophilia A for: On-demand treatment and control of bleeding episodes Perioperative management of bleeding Routine prophylaxis to reduce the frequency of bleeding episodes
Comparative agent – Therapeutic interchange?	Antihemophilic factor (recombinant), PEGylated (Adynovate)
Dosage forms/strengths. Common Dose/sig	Lyophilized powder in a single-use vial containing nominally 500, 1000, 2000, or 3000 IU Control of bleeding: Required dose (IU)= body weight (kg) x desired Factor VIII rise (% of normal or IU/dL) x reciprocal of expected recovery (or observed recovery, if available) Routine prophylaxis: 30-40 IU/kg twice weekly

antihemophilic factor (recombinant), PEGylated-aucl continued…	
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medication Names	Antihemophilic factor (recombinant), PEGylated (Adynovate)
Clinical Use Evaluation	
Common Adverse Effects	≥ 5%: headache, cough, nausea and fever
Severe Adverse Effects	Hypersensitivity reactions, neutralizing antibody formation, immune response to IgM anti-PEG antibodies
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.	- Monitoring for Factor VIII activity should be done using a validated chromogenic assay or a selected validated one-stage clotting assay - Monitor for development of Factor VIII inhibitors by performing a Bethesda inhibitor assay if expected Factor VIII plasma levels are not attained or if bleeding is not controlled with expected dose
Used in Pediatric Areas	Not for use in patients younger than 12 years of age
Renal or Hepatic Dosing	None reported
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in patients with hypersensitivity reactions to the active substance, polyethylene glycol (PEG), mouse or hamster proteins, or other constituents of the product. Warnings: - If hypersensitivity reactions occur, immediately discontinue administration and initiate appropriate treatment - Monitor for development of Factor VIII neutralizing antibodies - Immune response to PEG presents as acute hypersensitivity symptoms and/or loss of drug effect primarily in patients < 6 years of age; not for use in patients younger than 12 years due to greater risk for hypersensitivity reactions.
Special administration technique or considerations	Infuse over a period of 1 to 15 minutes; adapt the rate of administration to the response of each individual patient (maximum infusion rate of 2.5 mL/min).
Prepared by	Zach Diekmann & Brittany Craft
Source	Jivi (antihemophilic factor (recombinant), PEGylated-aucl). [prescribing information]. Whippany, NJ: Bayer HealthCare LLC; August 2018.