College of Pharmacy and Pharmaceutical Sciences
WASHINGTON STATE UNIVERSITY

Drug Information Center

Highlights of FDA Activities – 8/1/19 – 8/31/19

FDA Drug Safety Communications & Drug Information Updates:

Entacapone (*Comtan* & *Stalevo*) - Safety Update 8/13/19
In 2010 the FDA was informed of potential increases in the risk of prostate cancer with some Parkinson Disease medications, specifically *Comtan* (entacapone) and *Stalevo* (entacapone/carbidopa/levodopa). The FDA issued a report on August 13, 2019 stating that it found no evidence of increased prostate cancer risk with currently approved Parkinson drugs.

FDA Statement on Ongoing Efforts to Resolve Safety Issue with ARB Medications 8/28/19
The FDA provided an update on their continuing work regarding angiotensin receptor blockers (ARBs): clarifying the risk and scope of exposure, enhancing oversight of manufacturing data, and expanding the investigation. They are continuing to maintain the list of affected products and a list of 43 ARB medications that do not contain impurities.

Hepatitis C Medications – Serious Liver Injury 8/28/19
The FDA warned that rare cases of worsening liver function or liver failure have been reported following the use of *Mavyret* (glecaprevir/pibrentasvir), *Zepatier* (elbasvir/grazoprevir), or *Vosevi* (sofosbuvir/velpatasvir/voxilaprevir) in the treatment of chronic hepatitis C in patients with moderate to severe liver impairment. These agents are not approved for use in patients with moderate to severe liver impairment. Liver disease should be assessed at baseline, and these agents should continue to be prescribed as indicated for patients without liver impairment or with mild liver impairment.

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

PRE-TAT, Superior Pain and Itch Relief, & Soothing Sore Relief Creams and Gels by Pain Relief Naturally: Recall – Contamination and Superpotency 8/8/19
Ridge Products LLC, doing business as Pain Relief Naturally, recalled PRE-TAT cream and gel by TAT BALM 3-in-1 pre-tattoo prep with lidocaine, Superior Pain & Itch Releif [sic] cream and gel, and Soothing Sore Releif [sic] cream and gel products labeled as containing 4% lidocaine (lots 1135, 1222, 1213, and 1228) due to potential bacterial contamination and a higher than labeled concentration of lidocaine. Products were distributed through internet retailers such as Amazon, ebay, Walmart.com, tatbalm.net, and naturallyhl.com.

Vigilant A*gilia* Drug Library & *Volumat* MC Agilia Infusion Pump from Fresenius Kabi: Recall – Errors 8/12/19
A pre-programmed function of the infusion pump: "keep vein open (KVO)", when enabled, triggers an alarm and potentially causes the device to malfunction and provide subtherapeutic drug delivery. The manufacturer, Fresenius, has also identified several drug-library software errors in their products that may lead to medication dose errors. All *Volumat* infusion pumps and *Vigilant Drug Library* systems are affected by this recall.

Eletriptan hydrobromide (*Replax, Pfizer)* 40 mg Tablets: Recall – Potential Bacterial Contamination 8/15/19
Pfizer recalled lots AR5407 and CD4565 of *Replax* (eletriptan hydrobromide) 40 mg tablets due to potential bacterial contamination.

Drug Products Intended to be Sterile by *AmEx Pharmacy: Recall – Potential Contamination* 8/27/19
The FDA issued a warning regarding compounded products, notably ophthalmic agents, produced by AmEx pharmacy and its affiliated distributors due to deficient manufacturing processes. The FDA noted AmEx had been unwilling to voluntarily recall products intended to be sterile and had not made proper assurances involving future manufacturing processes.

Bevacizumab from AmEx Pharmacy: Recall – Potential Contamination 8/30/19

Pacifico National, doing business as AmEx Pharmacy, recalled all lots of bevacizumab 1.25 mg/0.05 mL 31G injectable and all lots of bevacizumab 2.5 mg/0.1 mL Normject TB injectable to the healthcare provider level following an FDA inspection. Recalled product is used for wet age-related macular degeneration and diabetic retinopathy and was distributed nationwide to ophthalmologist clinics.

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***
Miracle Mineral Solution (MMS) Miracle Mineral Supplement Master Mineral Solution Chlorine Dioxide (CD) Protocol Water Purification Solution (WPS)	Treating autism, cancer, HIV/AIDS, hepatitis, flu; water purification.	Bleach[1]

[1]Bleach has been shown to be a product of mixing MMS with water in some instances.

New Product Shortages	***Date Initially Posted***
Pentamidine isethionate solution for inhalation.	8/2/19

Product Discontinuations/Withdrawals	***Date Posted***
Epinastine hydrochloride (*Elestat*, Allergan) ophthalmic solution; remains available from generic manufacturers	8/19/19
Megestrol (*Megace ES*, Endo) 625 mg/5 mL oral suspension; remains available from generic manufacturers	8/21/19
Methocarbamol (*Robaxin*, Endo) 500 mg tablets; remains available from generic manufacturers	8/21/19
Testosterone buccal system (*Striant*, Endo) 30 mg; patients must be switched to an alternate testosterone dosage form	8/21/19

New Drug Approvals:	***Description (See Attached Drug Summaries)***	***Date Approved***
Pexidartinib / *Turalio* / Daiichi Sankyo, Inc	Kinase inhibitor indicated for the treatment of tenosynovial giant cell tumor	8/2/19
Pitolisant / *Wakix* / Bioprojet Pharmaceuticals	Dual agonist and antagonist to histamine 3, indicated for excessive daytime sleepiness in adults with narcolepsy	8/14/19
Pretomanid / TB Alliance	Antimycobacterial indicated, in combination with bedaquiline and linezolid, for pulmonary extensive drug-resistant (XDR), treatment intolerant, nonresponsive multiple drug-resistant (MDR) tuberculosis	8/14/19
Entrectinib / *Rozlytrek* / Genentech USA, Inc.	Kinase inhibitor indicated for adults with metastatic ROS1-positive non-small cell lung cancer and adults and pediatric patients 12 years and older with solid tumors with NTRK gene expression	8/15/19
Fedratinib / *Inrebic* / Celgene Corporation	Kinase inhibitor indicated for the treatment of adult patients with intermediate or high-risk primary or secondary myelofibrosis	8/16/19
Upadacitinib / *Rinvoq* / AbbVie Inc	Janus kinas inhibitor indicated for the treatment of adults with moderate-severe rheumatoid arthritis who have not responded to conventional treatments like methotrexate	8/16/19

New Drug Approvals: (continued)	***Description (See Attached Drug Summaries)***	***Date Approved***
Lefamulin / *Xenleta* / Nabriva Therapeutics Inc	Pleuromutilin antibacterial indicated for the treatment of adults with community acquired bacterial pneumonia caused by susceptible microorganisms	8/19/19
Ga 68 DOTATOC / UIHC PET Imaging	Diagnostic contrast imaging agent indicated for use with positron emission tomography (PET) for the localization and identification of somatostatin receptor positive neuroendocrine tumors in both adults and children	8/21/19
Istradefylline / *Nourianz* / Kyowa Kirin Inc	Nondopaminergic treatment of Parkinson's Disease "off periods" where levodopa inadequately controls symptoms	8/27/19

New Indications:	***Description***	***Date Approved***
Bedaquiline / *Situro* / Johnson & Johnson	Indication expanded to include treatment of tuberculosis in patients aged 12 years and older	8/12/19
RimabotulinumtoxinB / *Myobloc* / Solstice Neurosciences LLC	Treatment of chronic sialorrhea in adults	8/20/19
Cobicistat / *Tybost* / Gilead Sciences Inc	Indication expanded to include use with atazanavir in combination with other antiretroviral agents in the treatment of HIV-1 infection in pediatric patients weighing at least 35 kg	8/22/19
Ixekizumab / *Taltz* / Eli Lilly and Company	Treatment of adults with ankylosing spondylitis	8/23/19
Sofosbuvir / *Sovaldi* / Gilead	Indication expanded to include treatment of chronic hepatitis C virus, genotype 2 or 3 infection, in pediatric patients 3 years of age and older and weighing at least 17 kg	8/28/19
Ledipasvir and sofosbuvir / *Harvoni* / Gilead	Indication expanded to include treatment of chronic hepatitis C virus, genotype 1, 4, 5, or 6 infection, in pediatric patients 3 years of age and older and weighing at least 17 kg	8/28/19

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Ledipasvir and sofosbuvir oral pellets / *Harvoni* / Gilead	Oral pellets: 45 mg ledipasvir and 200 mg sofosbuvir; 33.75 mg ledipasvir and 150 mg sofosbuvir. Can be sprinkled on non-acidic soft food (eg pudding, chocolate syrup, mashed potato, ice cream) at or below room temperature. Swallow without chewing to avoid bitter aftertaste.	8/28/19
Sofosbuvir oral pellets / *Sovaldi* / Gilead	Oral pellets: 200 mg and 150 mg sofosbuvir. Can be sprinkled on non-acidic soft food (eg pudding, chocolate syrup, mashed potato, ice cream) at or below room temperature. Swallow without chewing to avoid bitter aftertaste.	8/28/19
Metformin extended-release suspension / *Riomet ER* / Sun Pharmaceuticals	Upon reconstitution, supplies 16 ounces of 500 mg/5 mL metformin as extended-release oral suspension. Both drug pellet bottle and drug diluent bottle contain metformin HCl; drug pellets are added to the supplied drug diluent bottle.	8/29/19

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Pexidartinib / *Turalio* / Daiichi Sankyo	
Generic Name / Brand Name / Company	Pexidartinib / *Turalio* / Daiichi Sankyo
Date of approval	8/2/19
Drug Class (Mechanism of Action if novel agent)	Kinase inhibitor; CSF1R Inhibitor
Indication	Treatment of tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to surgery
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths	Capsules: 200 mg
Common Dose/sig	400 mg orally twice daily
DEA Schedule	Not applicable
Date of market availability	Available; limited distribution program through a REMS
Similar Medication Names	*Pexeva*
Clinical Use Evaluation	
Common Adverse Effects	>20%: Increased LDH, increased AST, hair color changes, fatigue, increased ALT, decreased neutrophils, increased cholesterol, increased ALP, decreased lymphocytes, eye edema, decreased hemoglobin, rash, dysgeusia, and decreased phosphate.
Severe Adverse Effects	Hepatotoxicity (Black Box Warning)
Severe Drug-Drug Interactions	Avoid concomitant use with other hepatotoxic agents (i.e. acetaminophen), reduce pexidartinib dose with strong CYP3A inhibitors (increases pexidartinib plasma concentration), avoid use with strong CYP3A inducers (decreases concentration), reduce dose of pexidartinib with UGT inhibitors (increases concentration), and avoid proton-pump inhibitors (decreases concentration).
Severe Drug-Food Interactions	Alcohol consumption may increase hepatoxic effects of pexidartinib.
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Liver function tests including AST, ALT, ALP, GGT, and bilirubin; renal function. Laboratory test abnormalities require dose adjustment or discontinuation which can be found in the prescribing information.
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	Mild to moderate renal impairment (CrCl 15-89 mL/min): requires dose adjustment to 200 mg orally in the morning and 400 mg orally in the evening. Hepatic dosing: considerations based on liver function tests and/or signs of toxicity (see prescribing information).
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No labeled contraindications. Hepatotoxicity, including potentially fatal liver injury, has occurred. Pexidartinib is only available via a limited distribution program requiring prescriber and pharmacy certification and patient enrollment and inclusion in a registry. Potential for fetal harm: women of childbearing potential should use effective contraception during therapy and for 1 month after the final dose; males with female partners of reproductive potential should use effective contraception for the duration of treatment and 1 week following discontinuation.
Special administration technique or considerations	Administer pexidartinib on an empty stomach at least 1 hour before food or 2 hours following food. Swallow capsules whole.
Prepared by	Thomas James Borden
Source	*Turalio* (pexidartinib) [prescribing information]. Basking Ridge, NJ: Daiichi Sankyo, Inc; August 2019.

Pitolisant / *Wakix* / Bioprojet Pharma	
Generic Name / Brand Name / Company	Pitolisant / *Wakix* / Bioprojet Pharma
Date of approval	8/14/19
Drug Class (Mechanism of Action if novel agent)	Histamine 3 antagonist / inverse agonist.
Indication	Excessive daytime sleepiness (EDS) in adult patients with narcolepsy.
Comparative agent – Therapeutic interchange?	Modafinil, solriamfetol, methylphenidate, amphetamines
Dosage forms/strengths	Tablets: 4.45 mg, 17.8 mg
Common Dose/sig	Recommended dosage range: 17.8 to 35.6 mg once daily in the morning upon waking. Dose must be titrated: 8.9 mg daily for 7 days, then 17.8 mg daily, then 35.6 mg daily.
DEA Schedule	Not applicable
Date of market availability	4th quarter 2019
Similar Medication Names	Pitocin
Clinical Use Evaluation	
Common Adverse Effects	>5%: insomnia, nausea, anxiety
Severe Adverse Effects	QT prolongation
Severe Drug-Drug Interactions	Strong CYP2D6 inhibitors (eg, paroxetine, fluoxetine and bupropion) may increase serum levels of pitolisant; limit dose to 17.8 mg once daily. Strong CYP3A4 inducers (eg, rifampin, carbamazepine, and phenytoin) may decrease serum pitolisant levels. H1 receptor antagonists such as antihistamines and tricyclic antidepressants may reduce the efficacy of pitolisant. Concomitant use of medications that prolong QT interval; such as moxifloxacin, class 1A antiarrhythmics, class 3 antiarrhythmics, and some antipsychotics; may have additive effects with pitolisant and combinations should be avoided. Concomitant use of other CYP3A4 substrates should be used with caution (such as hormonal birth control, midazolam, cyclosporin) as pitolisant is a weak CYP3A4 inducer. Note: patients on hormonal birth control should use alternate non-hormonal methods during and for up to 21 days following pitolisant use.
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Renal and hepatic function at baseline.
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	Contraindicated in severe hepatic impairment; maximum dose is 17.8 mg once daily in moderate hepatic impairment. Maximum dose is 17.8 mg daily in moderate or severe renal impairment; not recommended in end stage renal disease.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in severe hepatic impairment. QT prolongation: avoid use in patients with known QT prolongation or in combination with drugs known to prolong the QT interval. Monitor for QT prolongation in patients with hepatic or renal impairment Limit dose to 17.8 mg once daily in patients known to be poor CYP2D6 metabolizers.
Special administration technique or considerations	Initiating pitolisant requires titration (see dosing).
Prepared by	Thomas James Borden
Source	*Wakix* (pitolisant) [prescribing information]. Paris, France: Bioprojet Pharma; August 2019.

Pretomanid / TB Alliance	
Generic Name / Brand Name / Company	Pretomanid / TB Alliance
Date of approval	8/14/19
Drug Class (Mechanism of Action if novel agent)	Nitroimidazooxazine antimycobacterial
Indication	In combination with bedaquiline and linezolid for the treatment of adults with pulmonary extensively drug resistant (XDR), treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths	Tablets: 200 mg
Common Dose/sig	200 mg daily for 26 weeks in combination with bedaquiline 400 mg daily for 14 days then 200 mg three times weekly for 24 weeks and linezolid 1200 mg daily for up to 26 weeks.
DEA Schedule	VI
Date of market availability	Not determined
Similar Medication Names	*Prandin*, pantoprazole, pregabalin
Clinical Use Evaluation	
Common Adverse Effects	≥10%: peripheral neuropathy, acne, anemia, nausea, vomiting, headache, increased transaminases, dyspepsia, reduced appetite, rash, pruritis, abdominal pain, pleural pain, increased gamma-glutamyltransferase, lower respiratory tract infection, hyperamylasemia, hemoptysis, back pain, cough, visual impairment, hypoglycemia, weight loss, QT prolongation, lactic acidosis, myelosuppression, hepatotoxicity and diarrhea.
Severe Adverse Effects	Peripheral and optical neuropathy, hepatotoxicity
Severe Drug-Drug Interactions	CYP3A4 inducers (eg, rifampin or efavirenz) decrease pretomanid serum concentrations; avoid strong or moderate inducers. Pretomanid may inhibit OAT3 transporters, which may increase the serum concentration of OAT3 substrates such as methotrexate.
Severe Drug-Food Interactions	Avoid alcohol use
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Prior to initiating therapy: liver function (ALT, AST, alkaline phosphatase, and bilirubin), complete blood count, serum potassium, calcium, and magnesium. Liver function tests, CBC at 2 weeks, then monthly.
Used in Pediatric Areas	Safety and efficacy not established in pediatric patients.
Renal or Hepatic Dosing	Insufficient studies have been performed to establish renal and/or hepatic dosing considerations.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in patients for whom bedaquiline or linezolid is contraindicated. Consider the cautions associated with each component of the regimen, in addition to those associated with pretomanid: Hepatotoxicity, myelosuppression, peripheral and optic neuropathy, QT prolongation, potential impaired male fertility.
Special administration technique or considerations	This medication must be taken in combination with linezolid and bedaquiline. Administer by directly observed therapy. Combination should be taken with food and plenty of water. Compliance is critical; doses of bedaquiline and pretomanid missed for safety reasons can be made up at the end of treatment. If any component of the regimen is discontinued, the entire combination regimen should be discontinued.
Prepared by	Thomas James Borden
Source	Pretomanid [prescribing information]. New York, NY: TB Alliance; August 2019.

Entrectinib / *Rozlytrek* / Genentech USA, Inc.	
Generic Name / Brand Name / Company	Entrectinib / *Rozlytrek* / Genentech USA, Inc.
Date of approval	8/15/19
Drug Class (Mechanism of Action if novel agent)	Tropomyosin kinase inhibitor (TRK); proto-oncogene tyrosine protein kinase inhibitor (ROS1); anaplastic lymphoma kinase inhibitor (ALK); JAK2 inhibitor; and TNK2 inhibitor.
Indication	Adults with metastatic small-cell lung cancer with positive ROS1 genotype and adults and pediatric patients 12 years and older with solid tumors expressing NTRK gene fusion, are metastatic or not amenable to surgery, and have progressed following treatment or with no treatment alternative
Comparative agent – Therapeutic interchange?	Crizotinib, larotrectinib
Dosage forms/strengths	Capsules: 100 mg, 200 mg
Common Dose/sig	Adults: 600 mg by mouth daily until progression or unacceptable toxicity. Pediatric patients: dosed by body surface area
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medication Names	Entocort, etanercept.
Clinical Use Evaluation	
Common Adverse Effects	≥20%: fatigue, constipation, dysgeusia, edema, dizziness, diarrhea, nausea, dysesthesia, cognitive impairment, weight gain, cough, vomiting, pyrexia, arthralgia, and visual disorders.
Severe Adverse Effects	Risk of congestive heart failure, cognitive impairment, skeletal fractures, hepatic toxicity, hyperuricemia, QT prolongation, visual disorders
Severe Drug-Drug Interactions	Moderate to strong CYP 3A4 inhibitors: decrease entrectinib dose or avoid. Moderate to strong CYP3A4 inducers: avoided with entrectinib. Avoid concomitant drugs that increase QT interval.
Severe Drug-Food Interactions	Avoid grapefruit (CYP3A inhibitor).
Important Lab Values to assess prior to order entry or at point of clinical follow up.	Liver function (ALT and AST) every 2 weeks for first month and then monthly. Uric acid and electrolytes prior to initiation and periodically.
Used in Pediatric Areas	Pediatric dosing is based on body surface area (BSA): children > 1.5 m^2 give 600 mg daily; children 1.11 to 1.50 m^2 give 500 mg daily; children 0.91 to 1.10 m^2 give 400 mg daily.
Renal or Hepatic Dosing	No adjustments recommended in mild to moderate renal impairment or mild hepatic impairment; not studied in severe renal impairment and moderate to severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No labeled contraindications. Congestive heart failure risk: assess left ventricular ejection fraction prior to initiation, monitor and adjust dose or discontinue if needed. Monitor for CNS effects, fractures, hepatotoxicity, hyperuricemia, QT prolongation, and vision disorders. Can cause fetal harm; females of reproductive potential should use effective contraception during therapy and for 5 week after final dose and males with female partners of reproductive potential should use effective contraception during treatment and for 3 months after the final dose.
Special administration technique or considerations	With or without food. Swallow capsules whole. Dose adjustments for adverse effects including congestive heart failure, CNS adverse effects, hepatotoxicity, hyperuricemia, QT prolongation, myelosuppression, vision changes.
Prepared by	Thomas James Borden
Source	*Rozlytrek* (entrectinib) [prescribing information]. San Francisco, CA: Genentech USA; August 2019.

Fedratinib / *Inrebic* / Celgene Corporation	
Generic Name / Brand Name / Company	Fedratinib / *Inrebic* / Celgene Corporation
Date of approval	8/16/19
Drug Class (Mechanism of Action if novel agent)	Kinase inhibitor; JAK2, FLT3
Indication	Adults with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis
Comparative agent – Therapeutic interchange?	Ruxolitinib – therapeutic alternative
Dosage forms/strengths	Capsules: 100 mg
Common Dose/sig	400 mg by mouth once daily (in patients with baseline platelet count greater than or equal to 50×10^9 / L)
DEA Schedule	Not applicable
Date of market availability	Not reported
Similar Medication Names	*Femhrt*, *Femara*
Clinical Use Evaluation	
Common Adverse Effects	>20%: diarrhea, nausea, anemia, vomiting
Severe Adverse Effects	Encephalopathy, including Wernicke's encephalopathy.
Severe Drug-Drug Interactions	Strong CYP3A4 inhibitors: reduce fedratinib dose. Strong and moderate CYP3A4 inducers: avoid fedratinib use. Dual CYP3A4 and CYP2C19 inhibitors: avoid fedratinib use.
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Assess at baseline and periodically: thiamine (Vit B1), CBC with platelets, creatinine with BUN, hepatic panel, amylase, and lipase.
Used in Pediatric Areas	Safety and effectiveness in pediatric patient populations has not been established.
Renal or Hepatic Dosing	Reduce to 200 mg by mouth daily in patients with severe renal impairment (CrCL 15 – 29 mL/min); no adjustments necessary in mild to moderate renal impairment. Avoid use in severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No labeled contraindications. Risk of encephalopathy, including Wernicke's encephalopathy which may be fatal. Monitor thiamine at baseline and periodically; replete prior to initiation. Discontinue if encephalopathy suspected. Monitor for anemia, thrombocytopenia, gastrointestinal toxicity, hepatotoxicity, and amylase and lipase elevations. Advise not to breastfeed.
Special administration technique or considerations	May be taken with or without food; however high-fat meals or snacks may reduce incidence of GI intolerance. Dose modifications for adverse effects: thrombocytopenia, neutropenia, nausea, vomiting, diarrhea, increased ALT, AST or bilirubin.
Prepared by	Thomas James Borden
Source	*Inrebic* (fedratinib) [prescribing information]. Summit, NJ: Celgene Corporation; August 2019.

Upadacitinib / *Rinvoq* / AbbVie Inc	
Generic Name / Brand Name / Company	Upadacitinib / *Rinvoq* / AbbVie Inc
Date of approval	8/16/19
Drug Class (Mechanism of Action if novel agent)	JAK Inhibitor
Indication	Adult patients with moderate-to-severe rheumatoid arthritis unresponsive to methotrexate or who are unable to tolerate methotrexate.
Comparative agent – Therapeutic interchange?	Baricitinib, tofacitinib
Dosage forms/strengths	Extended-release tablets: 15 mg
Common Dose/sig	15 mg by mouth once daily.
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medication Names	*UltraSept, Ultram*
Clinical Use Evaluation	
Common Adverse Effects	>1%: upper respiratory tract infection, nausea, cough, pyrexia
Severe Adverse Effects	Severe infection (including tuberculosis), malignancy, GI perforation, neutropenia, CPK elevation, transaminase elevation, thrombosis, lymphopenia, and anemia.
Severe Drug-Drug Interactions	Strong CYP3A4 inhibitors: use with caution. Strong CYP3A4 inducers: avoid concomitant use. Use in combination with other JAK inhibitors, biological DMARDs, or with potent immunosuppressive medications such as azathioprine and cyclosporin is not recommended. Avoid use with live vaccinations.
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	CBC and liver function tests prior to initiation and as recommended for routine patient management. Lipids at 12 weeks after initiation.
Used in Pediatric Areas	Safety and efficacy not established in pediatric patients
Renal or Hepatic Dosing	No renal dose adjustments required. Dose adjustment not required for mild or moderate hepatic impairment. Avoid use in severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No labeled contraindications. Avoid use in patients with active, serious infections and in patients with severe hepatic impairment. Screen for TB and viral hepatitis prior to initiation. Monitor for signs of infection, thrombosis, or malignancy; use with caution in patients at increased risk for gastrointestinal perforation. Women of reproductive potential should use effective contraception.
Special administration technique or considerations	With or without food. Swallow tablets whole. May be used as monotherapy or in combination with methotrexate or other nonbiologic DMARDs.
Prepared by	Thomas James Borden
Source	*Rinvoq* (upadacitinib) [prescribing information]. Chicago, IL: AbbVie Inc; August 2019.

Lefamulin / *Xenleta* / Nabriva Therapeutics US Inc.	
Generic Name / Brand Name / Company	Lefamulin / *Xenleta* / Nabriva Therapeutics US Inc.
Date of approval	8/19/19
Drug Class (Mechanism of Action if novel agent)	Pleuromutilin antibacterial; it inhibits bacterial protein synthesis through interactions with the A- and P- sites of the peptidyl transferase center (PTC) in domain V of the 23s rRNA of the 50s subunit. The binding pocket of the bacterial ribosome closes around the mutilin core for an induced fit that prevents correct positioning of tRNA.
Indication	Treatment of adults with community acquired bacterial pneumonia caused by susceptible organisms (*Streptococcus pneumoniae, Staphylococcus aureus (MSSA), Haemophilus influenzae, Legionella pneumophila, Mycoplasma pneumoniae, Chlamydophila pneumoniae*).
Comparative agent – Therapeutic interchange?	Antibacterials from other classes
Dosage forms/strengths	Injection: vial containing 150 mg of lefamulin in 15 mL of 0.9% sodium chloride for further dilution in supplied diluent prior to IV infusion. Tablets: 600 mg
Common Dose/sig	IV: 150 mg every 12 hours by IV infusion over 60 minutes Oral: 600 mg by mouth every 12 hours
DEA Schedule	Not applicable
Date of market availability	Mid-September 2019
Similar Medication Names	*Xarelto, Xenical, Xeloda, Xanax*
Clinical Use Evaluation	
Common Adverse Effects	≥2%: administration site reactions, hepatic enzyme elevation, nausea, hypokalemia, insomnia, headache, diarrhea, and vomiting.
Severe Adverse Effects	QT prolongation
Severe Drug-Drug Interactions	Strong and moderate CYP3A inducers or P-gp inducers: avoid if possible; strong and moderate CYP3A inhibitors or P-gp inhibitors: avoid if possible; CYP3A4 substrates that prolong QT interval: contraindicated; other sensitive CYP3A4 substrates: monitor for adverse reactions. Avoid use with meds known to prolong QT such as class IA and III antiarrhythmics, antipsychotics, erythromycin, moxifloxacin, and tricyclic antidepressants.
Severe Drug-Food Interactions	None listed
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Assess hepatic function prior to initiation
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients
Renal or Hepatic Dosing	Reduce the dose to 150 mg infused IV over 60 minutes every 24 hours for patients with severe hepatic impairment (Child-Pugh class C); no adjustments required with IV dosing for mild to moderate impairment. No dosage adjustment required for oral lefamulin in mild hepatic impairment; avoid use in moderate to severe hepatic impairment. No renal dosing adjustments required with IV or oral dosing.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: known sensitivity to lefamulin, concomitant use with CYP3A substrates that prolong QT interval Warnings: QT prolongation, embryo-fetal toxicity, *Clostridium difficile* associated diarrhea.
Special administration technique or considerations	Injection: infuse over 60 minutes Tablets: take 1 hour before or 2 hours after a meal and swallow whole with 6-8 ounces of water.
Prepared by	Alli Pettersen
Source	*Xenleta* (lefamulin) [prescribing information]. Ireland: Nabriva Therapeutics US, Inc.; August 2019.

Istradefylline / *Nourianz* / Kyowa Kirin Inc	
Generic Name / Brand Name / Company	Istradefylline / *Nourianz* / Kyowa Kirin Inc
Date of approval	8/27/19
Drug Class (Mechanism of Action if novel agent)	Adenosine A_{2a} receptor antagonist; precise mechanism unknown
Indication	Indicated for the treatment of Parkinson's Disease as an adjunct therapy with carbidopa-levodopa in those who experience "off" episodes
Comparative agent – Therapeutic interchange?	Alternatives: COMPT inhibitors and dopamine agonists
Dosage forms/strengths	Tablets: 20 mg, 40 mg
Common Dose/sig	20 mg orally once daily; may increase to maximum of 40 mg once daily
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medication Names	Itraconazole, isotretinoin, theophylline.
Clinical Use Evaluation	
Common Adverse Effects	≥5%: dyskinesia, dizziness, constipation, nausea, hallucinations, insomnia
Severe Adverse Effects	Dyskinesia, psychotic behavior, compulsive behavior
Severe Drug-Drug Interactions	Strong CYP3A4 inhibitors (eg ketoconazole): limit dose of istradefylline to 20 mg daily. Strong CYP3A4 inducer (eg rifampin, carbamazepine, phenytoin, St. John's Wort): avoid. CYP3A4 substrates (eg atorvastatin): monitor for adverse effects. P-gp substrates (eg digoxin): monitor for adverse effects.
Severe Drug-Food Interactions	Grapefruit juice should be avoided while taking istradefylline due to potential increases in bioavailability due to CYP3A4 inhibition.
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Liver function tests if suspected hepatic impairment. Monitor liver function during therapy if patient has moderate hepatic impairment.
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients.
Renal or Hepatic Dosing	Limit dose to 20 mg daily in those with moderate hepatic impairment; avoid use in those with severe hepatic impairment. No renal dose adjustments required.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No labeled contraindications. Monitor for dyskinesia, hallucinations, psychotic behavior, impulse control/compulsive behaviors. Dyskinesia was the most common cause of discontinuation of the medication. Monitor those with moderate hepatic impairment and limit dose to 20 mg daily in this population. It is recommended that those with severe hepatic impairment avoid using istradefylline. The recommended dose in patients who smoke 20 or more cigarettes per day (or equivalent tobacco intake) is 40 mg once daily.
Special administration technique or considerations	Take medication at the same time daily, with or without food, in conjunction with a levodopa-carbidopa dose.
Prepared by	Thomas James Borden
Source	*Nourianz* (istradefylline) prescribing information. Bedminster, NJ: Kyowo Kirin Inc.; August 2019.