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RX BENEFIT MANAGEMENT

PharmNOTES

Summary about new FDA products,
generic medication, medical products,
and WHAT IS IN THE PIPELINE.
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NEWS……

Drug Issue	Date	News/Event
FDA oversees destruction and recall of kratom products	02/21/2018	The FDA announced the voluntary destruction and recall of a large volume of kratom-containing dietary supplements manufactured and distributed nationwide under the brand names Botany Bay, Enhance Your Life and Divinity by Divinity Products Distribution of Grain Valley, Missouri. The scientific data about kratom provides evidence that compounds contained in kratom are opioids and are expected to have similar addictive effects as well as risks of abuse, overdose and, in some cases, death. At the same time, there's no evidence to indicate that kratom is safe or effective for any medical use. There are currently no FDA-approved therapeutic uses of kratom and importantly, the FDA has evidence to show that there are significant safety issues associated with its use. In cooperation with the FDA, the company has also agreed to stop selling all products containing kratom. Based on the scientific evidence of the serious risks associated with the use of kratom, in the interest of public health, the FDA encourages all companies currently involved in the sale of products containing kratom intended for human consumption to take similar steps to take their products off the market and submit any necessary evidence, as appropriate, to the FDA to evaluate them based on the applicable regulatory pathway. To protect the public health, consumers must be warned against the use of kratom-containing products.
Clarithromycin (Biaxin™): Potential Increased Risk of Heart Problems or Death in Patients With Heart Disease	02/22/2018	Clarithromycin is used to treat many types of infections affecting the skin, ears, sinuses, lungs, and other parts of the body, including Mycobacterium avium complex (MAC) infection, a type of lung infection that often affects people with human immunodeficiency virus (HIV). The FDA is advising caution before prescribing the antibiotic clarithromycin to patients with heart disease because of a potential increased risk of heart problems or death that can occur years later. The recommendation is based on a review of the results of a 10-year follow-up study of patients with coronary heart disease from the CLARICOR trial, which first observed this safety issue. Healthcare professionals should be aware of these significant risks and weigh the benefits and risks of clarithromycin before prescribing it to any patient, particularly in patients with heart disease and even for short periods, and consider using other available antibiotics. Advise patients with heart disease of the signs and symptoms of cardiovascular problems, regardless of the medical condition for which they are going to be treated with clarithromycin.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Biktarvy™ (bictegravir, emtricitabine and tenofovir alafenamide) Tablets, for oral use / Gilead Sciences, Inc.	Antiviral Integrase strand transfer inhibitor and emtricitabine/tenofovir alafenamide (Descovy™) combination, both HIV-1 nucleoside analog reverse transcriptase inhibitors	Treatment of HIV-1 infection in adults who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 3 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Biktarvy™ **Black box warning** Post treatment acute exacerbation of hepatitis B	02/07/2018	**DOSAGE AND ADMINISTRATION** The recommended dose is one tablet taken once daily. • Prior to or when initiating Biktarvy™ test for hepatitis B virus infection. Prior to or when initiating Biktarvy™, and during treatment, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients as clinically appropriate. In patients with chronic kidney disease, also assess serum phosphorus. • Is not recommended in patients with estimated creatinine clearance below 30 mL per minute and/or with severe hepatic impairment. **DOSAGE FORMS AND STRENGTHS** Tablets: 50 mg of bictegravir (equivalent to 52.5 mg of bictegravir sodium), 200 mg of emtricitabine, and 25 mg of tenofovir alafenamide (equivalent to 28 mg of tenofovir alafenamide fumarate). **CONTRAINDICATIONS** • Co-administration with: dofetilide and/or rifampin. **WARNINGS AND PRECAUTIONS** • **Black box warning:** Severe acute exacerbations of hepatitis B have been reported in patients who are co-infected with HIV-1 and hepatitis B virus (HBV) and have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of Biktarvy™. Closely monitor hepatic in patients who are co-infected. If appropriate, anti-hepatitis B therapy may be warranted.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Biktarvy™ (bictegravir, emtricitabine and tenofovir alafenamide) Tablets, for oral use / Gilead Sciences, Inc. (continuation)	Antiviral Integrase strand transfer inhibitor and emtricitabine/tenofovir alafenamide (Descovy™) combination, both HIV-1 nucleoside analog reverse transcriptase inhibitors	Treatment of HIV-1 infection in adults who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 3 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Biktarvy™ **Black box warning** Post treatment acute exacerbation of hepatitis B	02/07/2018	**WARNINGS AND PRECAUTIONS** (continuation) • **Hepatic:** (1) Severe acute exacerbation of hepatitis B in patients co-infected with HIV-1 and HBV has been reported after discontinuation of emtricitabine or tenofovir disoproxil fumarate; screen for HBV before or when initiating antiretroviral therapy. Monitoring recommended and anti-hepatitis B therapy may be warranted upon discontinuation, especially in patients with advanced liver disease or cirrhosis. (2) Lactic acidosis and severe hepatomegaly with steatosis, including fatalities, have been reported with emtricitabine or tenofovir alone or in combination with other antiretrovirals; suspend treatment if pronounced hepatotoxicity (including hepatomegaly or steatosis) or lactic acidosis develops, even if transaminases do not markedly increase. • **Immunologic:** (1) Autoimmune disorders (e.g. Graves' disease, Guillain-Barré syndrome, polymyositis) have been reported in the setting of immune reconstitution. (2) Immune reconstitution syndrome, leading to inflammatory response to indolent or residual infections, has been reported. • **Renal:** New onset or worsening renal impairment, including acute renal failure and Fanconi syndrome, has been reported; increased risk with impaired renal function and use of nephrotoxic agents; monitoring recommended before and during therapy. Discontinuation may be necessary. **ADVERSE REACTIONS** Most common adverse reactions: diarrhea, nausea, and headache. **DRUG INTERACTIONS** • **Other antiretroviral medications:** Because Biktarvy™ is a complete regimen, co-administration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended

New FDA Approved Products

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Biktarvy™ (bictegravir, emtricitabine and tenofovir alafenamide) Tablets, for oral use / Gilead Sciences, Inc. (continuation)	Antiviral Integrase strand transfer inhibitor and emtricitabine/tenofovir alafenamide (Descovy™) combination, both HIV-1 nucleoside analog reverse transcriptase inhibitors	Treatment of HIV-1 infection in adults who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 3 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Biktarvy™ **Black box warning** Post treatment acute exacerbation of hepatitis B	02/07/2018	**DRUG INTERACTIONS** (continuation) See Full Prescribing Information prior to and during treatment for other important drug interactions. **USE IN SPECIFIC POPULATIONS** • **Lactation:** Women infected with HIV should be instructed not to breastfeed due to the potential for HIV transmission. • **Pediatric use:** Safety and effectiveness of in pediatric patients less than 18 years of age have not been established. • **Geriatric use:** Clinical trials did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Dexycu™ (dexamethasone) Suspension, for intraocular use / Icon Bioscience Inc.	Long-acting corticosteroid	Treatment of postoperative inflammation associated with cataract surgery	02/09/2018	**DOSAGE AND ADMINISTRATION** The recommended dose is to administer 0.005 mL into the posterior intraocular chamber inferiorly behind the iris at the end of ocular surgery. **DOSAGE FORMS AND STRENGTHS** Intraocular suspension: 9% equivalent to dexamethasone 103.4 mg/mL in a single-dose vial provided in a kit. **CONTRAINDICATIONS** None. **WARNINGS AND PRECAUTIONS** • **Increase in intraocular pressure (IOP):** Monitor for increases in IOP. • **Delayed Healing:** Monitor for delayed healing. • **Infection Exacerbation:** Monitor and treat for any exacerbations of bacterial, viral or fungal infections. • **Cataract Progression:** Cataracts may develop or progress in phakic patients. **ADVERSE REACTIONS** Most common adverse reactions: intraocular pressure increased, corneal edema and iritis. **USE IN SPECIFIC POPULATIONS** • **Pediatric use:** Safety and effectiveness in pediatric patients have not been established. • **Geriatric use:** No overall differences in safety or effectiveness have been observed between older and younger patients.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Symdeko™ (ivacaftor/tezacaftor and ivacaftor) Tablets, for oral use / Vertex Pharmaceuticals Incorporated	Respiratory agent Cystic fibrosis transmembrane conductance regulator (CFTR) potentiator and CFTR corrector combination	Treatment of cystic fibrosis (CF) in patients aged 12 years and older who have two copies of the *F508del* mutation (homozygous), or who have at least one mutation in the CF gene that is responsive to treatment with Symdeko™ r based on in vitro data and/or clinical evidence	02/12/2018	**DOSAGE AND ADMINISTRATION** The recommended dose for adults and pediatric patients ages 12 years and older is one tablet (containing tezacaftor 100 mg/ivacaftor 150 mg) in the morning and one tablet (containing ivacaftor 150 mg) in the evening, approximately 12 hours apart. • Should be taken with fat-containing food. • Reduce dose in patients with moderate and severe hepatic impairment. • Reduce dose when co-administered with drugs that are moderate or strong CYP3A inhibitors. **DOSAGE FORMS AND STRENGTHS** Tablets: Symdeko™ is co-packaged as tezacaftor 100 mg/ivacaftor 150 mg fixed dose combination tablets and ivacaftor 150 mg tablets. **CONTRAINDICATIONS** None. **WARNINGS AND PRECAUTIONS** • **Concomitant use:** Concomitant use with strong CYP3A inducers (e.g. rifampin, St. John's wort) substantially decrease exposure of ivacaftor and may decrease the exposure of tezacaftor, which may reduce therapeutic effectiveness. Therefore, co-administration is not recommended. • **Hepatic:** Elevated transaminases (ALT or AST) have been reported. Transaminases (ALT and AST) should be assessed prior to initiating, every 3 months during the first year of treatment, and annually thereafter. In patients with a history of transaminase elevations, more frequent monitoring should be considered. Dosing should be interrupted in patients with significant elevations of transaminases (e.g. patients with ALT or AST >5 x upper limit of normal (ULN), or ALT or AST >3 x ULN with bilirubin >2 x ULN). Following resolution of transaminase elevations, consider the benefits and risks of resuming treatment.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Symdeko™ (ivacaftor/tezacaftor and ivacaftor) Tablets, for oral use / Vertex Pharmaceuticals Incorporated (continuation)	Respiratory agent Cystic fibrosis transmembrane conductance regulator (CFTR) potentiator and CFTR corrector combination	Treatment of cystic fibrosis (CF) in patients aged 12 years and older who have two copies of the *F508del* mutation (homozygous), or who have at least one mutation in the CF gene that is responsive to treatment with Symdeko™ r based on in vitro data and/or clinical evidence	02/12/2018	**WARNINGS AND PRECAUTIONS** (continuation) • **Ophthalmic:** Non-congenital lens opacities/cataracts have been reported in pediatric patients treated with Symdeko™. Baseline and follow-up examinations are recommended in pediatric patients initiating treatment. **ADVERSE REACTIONS** Most common adverse reactions: headache, nausea, sinus congestion, and dizziness. **DRUG INTERACTIONS** • **CYP3A inducers:** Tezacaftor and ivacaftor are substrates of CYP3A (ivacaftor is a sensitive substrate of CYP3A). Concomitant use of CYP3A inducers may result in reduced exposures and thus reduced efficacy. Co-administration of ivacaftor with rifampin, a strong CYP3A inducer, significantly decreased ivacaftor exposure by 89%. Tezacaftor exposures can also be expected to decrease significantly during co-administration with strong CYP3A inducers. Therefore, co-administration with strong CYP3A inducers is not recommended. • **CYP3A inhibitors:** Reduce Symdeko™ dose when co-administered with strong (e.g. ketoconazole) or moderate (e.g. fluconazole) CYP3A inhibitors. Avoid food containing grapefruit or Seville oranges. **USE IN SPECIFIC POPULATIONS** • **Pediatric use:** Safety and efficacy of in patients with CF younger than 12 years of age have not been studied. • **Geriatric use:** Clinical trials of did not include sufficient numbers of patients 65 years of age and over to determine whether they respond differently from younger patients.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Symdeko™ (ivacaftor/tezacaftor and ivacaftor) Tablets, for oral use / Vertex Pharmaceuticals Incorporated (continuation)	Respiratory agent Cystic fibrosis transmembrane conductance regulator (CFTR) potentiator and CFTR corrector combination	Treatment of cystic fibrosis (CF) in patients aged 12 years and older who have two copies of the *F508del* mutation (homozygous), or who have at least one mutation in the CF gene that is responsive to treatment with Symdeko™ r based on in vitro data and/or clinical evidence	02/12/2018	**USE IN SPECIFIC POPULATIONS** (continuation) • **Hepatic impairment:** No dose adjustment is necessary for patients with mild hepatic impairment (Child-Pugh Class A). A reduced dose is recommended in patients with moderate hepatic impairment (Child-Pugh Class B). There is no experience in patients with severe hepatic impairment (Child-Pugh Class C), but tezacaftor/ivacaftor exposure is expected to be higher than in patients with moderate hepatic impairment. Therefore, use with caution at a reduced dose in patients with severe hepatic impairment after weighing the risks and benefits of treatment. • **Renal impairment:** Has not been studied in patients with moderate or severe renal impairment or in patients with end-stage renal disease. No dose adjustment is recommended for mild and moderate renal impairment. Caution is recommended in patients with severe renal impairment or end-stage renal disease

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Erleada™ (apalutamide) Tablets, for oral use / Janssen Pharmaceuticals, Inc.	Antineoplastic agent Androgen receptor inhibitor	Treatment of men with non-metastatic castration-resistant prostate cancer (CRPC)	02/14/2018	**DOSAGE AND ADMINISTRATION** The recommended dose is 240 mg (four 60 mg tablets) once daily. • Patients should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy. **DOSAGE FORMS AND STRENGTHS** Tablets: 60 mg. **CONTRAINDICATIONS** • Pregnancy. **WARNINGS AND PRECAUTIONS** • **Musculoskeletal:** Falls and fractures have occurred; evaluate all patients for risk, monitoring and management may be required. • **Neurologic:** Seizure has occurred; permanently discontinue use. **ADVERSE REACTIONS** Most common adverse reactions: e fatigue, hypertension, rash, diarrhea, nausea, weight decreased, arthralgia, fall, hot flush, decreased appetite, fracture, and peripheral edema. **DRUG INTERACTIONS** • **Medications that are sensitive substrates of CYP3A4, CYP2C19, CYP2C9, UGT, P-gp, BCRP, or OATP1B1:** Concomitant use may result in loss of activity of these medications.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Erleada™ (apalutamide) Tablets, for oral use / Janssen Pharmaceuticals, Inc. (continuation)	Antineoplastic agent Androgen receptor inhibitor	Treatment of men with non-metastatic castration-resistant prostate cancer (CRPC)	02/14/2018	**USE IN SPECIFIC POPULATIONS** • **Pregnancy:** Erleada™ is not indicated for use in females and it is contraindicated for use in pregnant women because the drug can cause fetal harm and potential loss of pregnancy. • **Males of Reproductive Potential:** Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose. • **Pediatric use:** Safety and effectiveness in pediatric patients have not been established. • **Geriatric use:** No overall differences in effectiveness were observed between patients 65 years or older and younger patients.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Osmolex ER™ (amantadine hydrochloride) Extended-Release Tablets / Osmotica Pharmaceutical US LLC	Anticholinergic agent	Treatment of Parkinson's disease and drug-induced extrapyramidal reactions in adult patients	02/20/2018	**DOSAGE AND ADMINISTRATION** The recommended initial dose is 129 mg orally once daily in the morning. The dosage may be increased in weekly intervals to a maximum daily dose of 322 mg once daily in the morning. • Dosing frequency reduction and monitoring required for renal impairment. **DOSAGE FORMS AND STRENGTHS** Extended release tablets containing 129 mg, 193 mg, or 258 mg amantadine. **CONTRAINDICATIONS** • End stage renal disease. • Hypersensitivity to amantadine hydrochloride or to other components of the product. **WARNINGS AND PRECAUTIONS** • **Falling asleep during activities of daily living and somnolence:** Advise patients prior to treatment; ordinarily discontinue if occurs. • **Suicidality and depression:** Monitor patients for depressed mood, depression, or suicidal ideation or behavior. • **Hallucinations/Psychotic behavior:** Patients with major psychotic disorder should ordinarily not be treated with Osmolex™ ER; observe patients for the occurrence of hallucinations throughout treatment, especially at initiation and after dose increases. • **Dizziness and orthostatic hypotension:** Monitor patients for dizziness and orthostatic hypotension, especially after starting Osmolex™ ER or increasing the dose. • **Withdrawal emergent hyperpyrexia and confusion:** Avoid sudden discontinuation. • **Impulse control/Compulsive behaviors:** Ask patients about increased gambling urges, sexual urges, uncontrolled spending or other urges; consider dose reduction or discontinuation if occurs.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Osmolex ER™ (amantadine hydrochloride) Extended-Release Tablets / Osmotica Pharmaceutical US LLC (continuation)	Anticholinergic agent	Treatment of Parkinson's disease and drug-induced extrapyramidal reactions in adult patients	02/20/2018	**ADVERSE REACTIONS** Most common adverse reactions: nausea, dizziness lightheadedness, and insomnia. **DRUG INTERACTIONS** • **Anticholinergic drugs:** Increased risk of anticholinergic effects he dose of anticholinergic drugs or Osmolex™ ER may require reduction. • **Drugs affecting urinary pH:** Excretion increases with acidic urine; possible accumulation with urine change towards alkaline. • **Live attenuated influenza vaccines:** Not recommended during use. • **Alcohol:** Concomitant use is not recommended; increased potential for CNS effects. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** May cause fetal harm. • **Pediatric use:** Safety and effectiveness in pediatric patients have not been established. • **Geriatric use:** No dose adjustment is recommended on the basis of age. Osmolex™ ER is known to be substantially excreted by the kidney, and the risk of adverse reactions may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. • **Renal impairment:** Amantadine is mainly excreted in the urine, so it accumulates in the plasma and in the body when renal function declines. Osmolex™ ER is contraindicated for use in patients with end-stage renal disease. For patients with moderate or severe renal impairment, a reduction in dosing frequency is required. Closely monitor these patients if prescribed the maximum daily dosage of 322 mg. Also, closely monitor patients with any degree of renal impairment for adverse reactions and potential changes in renal function, which may necessitate further dosage reduction.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Apadaz™ (acetamino-phen and benzhydrocodone hydrochloride), for oral use / KemPharm, Inc.	Narcotic analgesic combination Note: Schedule II controlled substance	Short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate **Limitations of use:** Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Apadaz™ for use in patients for whom alternative treatment options [e.g., non-opioid analgesics] have not been or are not expected tolerated, or have not provided adequate analgesia, or are not expected to provide adequate analgesia **Black box warning** Addiction, abuse, and misuse; life-threatening respiratory depression; accidental ingestion; neonatal opioid withdrawal syndrome; cytochrome P450 3A4 interaction; hepatotoxicity; and risks from concomitant use with benzodiazepines or other CNS depressants	02/23/2018	**DOSAGE AND ADMINISTRATION** The recommended initial dose is 1 or 2 tablets every 4 to 6 hours as needed for pain. Dosage should not exceed 12 tablets in a 24 hour period. • Lowest effective dose should be used for the shortest duration consistent with individual patient treatment goals. • Dosing should be individualized based on the severity of pain, patient response, prior analgesic experience, and risk factors for addiction, abuse, and misuse. **DOSAGE FORMS AND STRENGTHS** Immediate-release tablets: 6.12 mg benzhydrocodone (equivalent to 6.67 mg benzhydrocodone hydrochloride) and 325 mg acetaminophen. **CONTRAINDICATIONS** • Significant respiratory depression. • Acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment. • Known or suspected gastrointestinal obstruction, including paralytic ileus. • Hypersensitivity to hydrocodone or acetaminophen. **WARNINGS AND PRECAUTIONS** • **Addiction:** Addiction may occur in patients at recommended doses; assess risk prior to initiating therapy. Increased risk in patients with personal or familial history of substance abuse or mental illness. • **Cardiovascular:** (1) Severe hypotension, including orthostatic hypotension and syncope, has been reported in ambulatory patients, with an increased risk in patients with reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g. phenothiazines or general anesthetics); monitoring recommended. (2) Avoid use in patients with circulatory shock.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Apadaz™ (acetaminophen and benzhydrocodone hydrochloride), for oral use / KemPharm, Inc. (continuation)	Narcotic analgesic combination Note: Schedule II controlled substance	Short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate **Limitations of use:** Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Apadaz™ for use in patients for whom alternative treatment options [e.g., non-opioid analgesics] have not been or are not expected tolerated, or have not provided adequate analgesia, or are not expected to provide adequate analgesia **Black box warning** Addiction, abuse, and misuse; life-threatening respiratory depression; accidental ingestion; neonatal opioid withdrawal syndrome; cytochrome P450 3A4 interaction; hepatotoxicity; and risks from concomitant use with benzodiazepines or other CNS depressants	02/23/2018	**WARNINGS AND PRECAUTIONS** (continuation) • **Concomitant use:** Avoid concomitant use of full opioid agonist analgesic and mixed agonist/antagonist (e.g. pentazocine, nalbuphine, and butorphanol) or partial agonist (e.g. buprenorphine) analgesics as decreased efficacy or potentially withdrawal may result. Dose adjustment may be necessary. • **Dermatologic:** Serious skin reactions, including acute generalized exanthematous pustulosis, Stevens-Johnson Syndrome, and toxic epidermal necrolysis, may rarely occur with acetaminophen use; discontinue if condition or other sign of hypersensitivity occurs. • **Endocrine and metabolic:** Adrenal insufficiency has been reported, generally with opioid use of 1 month or longer; if condition suspected, confirm with diagnostic testing. If diagnosed, treat with corticosteroids and wean patient off of opioid. • **Hepatic:** Spasm of the sphincter of Oddi may occur; monitor patients with biliary tract diseases, including acute pancreatitis, for worsening symptoms. • **Immunologic:** Hypersensitivity reactions and anaphylaxis, requiring emergency medical attention, have been reported; discontinue use if condition occurs. • **Neurologic:** (1) Further increases in intracranial pressure caused by benzhydrocodone-induced respiratory depression and CO2 retention may occur in patients with increased intracranial pressure or brain tumors; monitoring recommended especially during therapy initiation. (2) Neurologic: Clinical course may be obscured in patients with head injury. (3) Avoid use in patients with impaired consciousness or coma. (4) Increased risk of seizures and frequency of seizures in patients with seizure disorders; monitoring recommended. (5) Cognition and motor function may be impaired; advise patient to avoid driving and avoid operating dangerous machinery until the effects of drug are known.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Apadaz™ (acetaminophen and benzhydrocodone hydrochloride), for oral use / KemPharm, Inc. (continuation)	Narcotic analgesic combination Note: Schedule II controlled substance	Short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate **Limitations of use:** Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Apadaz™ for use in patients for whom alternative treatment options [e.g., non-opioid analgesics] have not been or are not expected tolerated, or have not provided adequate analgesia, or are not expected to provide adequate analgesia **Black box warning** Addiction, abuse, and misuse; life-threatening respiratory depression; accidental ingestion; neonatal opioid withdrawal syndrome; cytochrome P450 3A4 interaction; hepatotoxicity; and risks from concomitant use with benzodiazepines or other CNS depressants	02/23/2018	**WARNINGS AND PRECAUTIONS** (continuation) • **Respiratory:** Increased risk of decreased respiratory drive, including apnea, in patients with significant chronic obstructive pulmonary disease or cor pulmonale, and substantially decreased respiratory reserve, hypoxia, hypercapnia, or preexisting respiratory depression; monitoring recommended especially with therapy initiation, dosage titration, or when concomitantly administered with other drugs that depress respiration. • **Special Populations:** Increased risk of life-threatening respiratory depression in elderly, cachectic, or debilitated patients; monitoring recommended especially with therapy initiation, dosage titration, or when concomitantly administered with other drugs that depress respiration. • **Withdrawal:** Avoid abrupt discontinuation of therapy; gradually taper dose **ADVERSE REACTIONS** Most common adverse reactions: nausea, somnolence, vomiting, constipation, pruritus, dizziness, and headache **DRUG INTERACTIONS** • **Serotonergic Drugs:** Concomitant use may result in serotonin syndrome. Discontinue Apadaz™ if serotonin syndrome is suspected. • **Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics:** Avoid use with Apadaz™ because they may reduce analgesic effect of Apadaz™ or precipitate withdrawal symptoms. • **Monoamine Oxidase Inhibitors (MAOIs):** Can potentiate the effects of hydrocodone. Avoid concomitant use in patients receiving MAOIs or within 14 days of stopping treatment with an MAOI.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Apadaz™ (acetaminophen and benzhydrocodone hydrochloride), for oral use / KemPharm, Inc. (continuation)	Narcotic analgesic combination Note: Schedule II controlled substance	Short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate **Limitations of use:** Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Apadaz™ for use in patients for whom alternative treatment options [e.g., non-opioid analgesics] have not been or are not expected tolerated, or have not provided adequate analgesia, or are not expected to provide adequate analgesia **Black box warning** Addiction, abuse, and misuse; life-threatening respiratory depression; accidental ingestion; neonatal opioid withdrawal syndrome; cytochrome P450 3A4 interaction; hepatotoxicity; and risks from concomitant use with benzodiazepines or other CNS depressants	02/23/2018	**USE IN SPECIFIC POPULATIONS** • **Pregnancy:** May cause fetal harm. • **Lactation:** Hydrocodone and acetaminophen are present in human milk. Infants exposed to Apadaz™ through breast milk should be monitored for excess sedation and respiratory depression. Withdrawal symptoms can occur in breastfed infants when maternal administration of an opioid analgesic is stopped, or when breast-feeding is stopped. • **Pediatric use:** Safety and effectiveness in pediatric patients below the age of 18 years have not been established. • **Geriatric use:** Elderly patients (aged 65 years or older) may have increased sensitivity to hydrocodone.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Ztlido™ (lidocaine topical system) Patch, for transdermal use / Scilex Pharmaceuticals, Inc.	Anesthetic	Treatment of post-herpetic neuralgia	02/28/2018	**DOSAGE AND ADMINISTRATION** One Ztlido™ (lidocaine topical system) 1.8% provides equivalent lidocaine exposure to one Lidoderm (lidocaine patch 5%). **DOSAGE FORMS AND STRENGTHS** Ztlido™ 1.8% is available as a single-use topical system. **CONTRAINDICATIONS** • Known history of sensitivity to local anesthetics of the amide type, or to any other component of the product. **WARNINGS AND PRECAUTIONS** • **Accidental Exposure:U**Even a used Ztlido™ topical system contains residual lidocaine after use. It is important for patients to store and dispose of Ztlido™ properly and keep out of the reach of children, pets, and others. • **Excessive Dosing/Overexposure:** Applying Ztlido™ to larger surface areas or for a longer duration than recommended could lead to increased absorption and high blood concentrations of lidocaine, leading to adverse effects. • **Increased Absorption on Non-Intact Skin:** May result in higher blood concentrations of lidocaine. • **Risk of Overexposure with External Heat Sources:** Applying external heat sources to Ztlido™ may result in increased drug exposure. • **Application Site Reactions:** During or immediately after treatment Ztlido™, application site reactions may develop. • **Hypersensitivity Reactions:** Cross sensitivity to Ztlido™ in patients with a history of drug sensitivity to para-aminobenzoic acid (PABA) derivatives is possible. • **Eye Exposure:** Immediately wash out the eye with water or saline and protect the eye until sensation returns.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Ztlido™ (lidocaine topical system) Patch, for transdermal use / Scilex Pharmaceuticals, Inc. (continuation)	Anesthetic	Treatment of post-herpetic neuralgia	02/28/2018	**ADVERSE REACTIONS** Most common adverse reactions: irritation, erythema, and pruritus. **DRUG INTERACTIONS** • **Class I Antiarrhythmic Drugs:** When Ztlido™ is used in patients receiving Class I antiarrhythmic drugs (e.g. tocainide and mexiletine) the toxic effects are additive and potentially synergistic. Consider risk/benefit before concomitant use. • **Local Anesthetic Agents:** When Ztlido™ is used concomitantly with other products containing local anesthetic agents, the effects are additive. Consider the amount of drug absorbed from all formulations when local anesthetics are administered concomitantly. **USE IN SPECIFIC POPULATIONS** • **Lactation:** Lidocaine is excreted into human milk. Caution should be exercised when Ztlido™ is administered to a nursing mother, especially when administered with other local anesthetics. • **Pediatric use:** Safety and effectiveness in pediatric patients have not been established. • **Geriatric use:** Clinical studies of Ztlido™ did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be done with caution, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Avycaz™ (avibactam and ceftazidime) Injection / Actavis Pharma, Inc.	Antibiotic Next generation, non-β lactam β-lactamase inhibitor and third-generation, antipseudomonal cephalosporin antibiotic combination	Treatment of complicated intra-abdominal infections, complicated urinary tract infections, hospital-acquired bacterial pneumonia, and ventilator-associated bacterial pneumonia **New indication:** For the treatment of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) caused by the following susceptible Gram-negative microorganisms: *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Escherichia coli*, *Serratia marcescens*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae* in patients 18 years of age or older	02/01/2018	The approval is based on data from a Phase 3 study evaluating the efficacy and safety of Avycaz™ for the treatment of adult patients with HABP/VABP. A total of 870 hospitalized adult patients with HABP or VABP were randomized. The primary efficacy endpoint of the study was 28-day all-cause mortality (28 to 32 days after randomization). The study demonstrated that Avycaz™ was non-inferior to meropenem with respect to the primary endpoint based on a 10% non-inferiority margin; the 28-day all-cause mortality rate was 9.6% (42/436) in patients treated with Avycaz™ compared with 8.3% (36/434) in meropenem treated patients. This is the third therapeutic indication for Avycaz™. Avycaz™ was first approved for the treatment of adult patients with complicated intra-abdominal infections (cIAI), in combination with metronidazole, and later for complicated urinary tract infections (cUTI), including pyelonephritis, caused by designated susceptible Gram-negative bacteria, including certain Enterobacteriaceae and *Pseudomonas aeruginosa*.
Feraheme™ (ferumoxytol) Intravenous Injection / AMAG Pharmaceuticals, Inc.	Iron replacement therapy	Treatment of iron deficiency anemia (IDA) in adult patients **New indication:** To broaden the existing label beyond the current chronic kidney disease (CKD) indication to include all eligible adult IDA patients who have intolerance to oral iron or have had unsatisfactory response to oral iron	02/05/2018	The approval was supported by two Phase 3 trials evaluating Feraheme™ versus iron sucrose or placebo in a broad population of patients with IDA. It was also supported by positive results from a third Phase 3 trial comparing Feraheme™ to Injectafer™ (ferric carboxymaltose injection) in approximately 2,000 adults with IDA. The study demonstrated comparability to Injectafer™ based on the primary composite endpoint of the incidence of moderate-to-severe hypersensitivity reactions (including anaphylaxis) and moderate-to-severe hypotension. The study also met important secondary safety and efficacy endpoints, including the demonstration of mean improvement in hemoglobin per gram of iron administered from baseline to week 5 (1.35 g/dL Feraheme™ versus 1.10 g/dL Injectafer™).

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Zytiga™ (abiraterone) Tablets / Centocor Ortho Biotech Inc.	Antineoplastic agent CYP17 inhibitor	Treatment of patients with metastatic castration-resistant prostate cancer and metastatic high-risk castration-sensitive prostate cancer (CSPC) **New indication:** In combination with prednisone for the treatment of patients with metastatic high-risk CSPC	02/08/2018	The approval is based on Phase 3 data from the LATITUDE clinical trial, which found that in patients with metastatic high-risk CSPC, Zytiga™ in combination with prednisone reduced the risk of death by 38% compared to placebo.
Imfinzi™ (durvalumab) Injection / AstraZeneca	Antineoplastic agent Anti-PD-L1 (programmed death ligand-1) human monoclonal antibody	Treatment of patients with metastatic urothelial carcinoma and for the treatment of patients with unresectable non-small cell lung cancer (NSCLC) that has not progressed after chemoradiation **New indication:** Treatment of patients with stage III NSCLC whose tumors are not able to be surgically removed (unresectable) and whose cancer has not progressed after treatment with chemotherapy and radiation (chemoradiation)	02/16/2018	This approval makes Imfinzi™ the first treatment approved for stage III unresectable NSCLC to reduce the risk of the cancer progressing, when the cancer has not worsened after chemoradiation. For patients with stage III lung cancer that cannot be removed surgically, the current approach to prevent progression is chemoradiation. Although a small number of patients may be cured with the chemoradiation, the cancer may eventually progress. Patients now have an approved therapy that has been shown to keep the cancer from progressing for a longer time after chemoradiation. Imfinzi™ was previously approved in May 2017 for the treatment of certain patients with locally advanced or metastatic bladder cancer. The approval of Imfinzi™ for the treatment of stage III, unresectable NSCLC was based on a randomized trial of 713 patients whose cancer had not progressed after completing chemotherapy and radiation. The trial measured the length of time the tumors did not have significant growth after starting treatment with Imfinzi™ or a placebo (progression-free survival). The median progression-free survival for patients taking Imfinzi™ was 16.8 months compared to 5.6 months for patients receiving a placebo. In addition, the Post-marketing, additional information about how long patients lived following treatment with Imfinzi™ after chemotherapy and radiation (overall survival) will be provided.

New FDA Approved Indications

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Verzenio™ (abemaciclib) Tablets / Eli Lilly and Company	Antineoplastic agent Selective ATP-competitive inhibitor of cyclin dependent kinases (CDK) 4 and 6	Treatment of metastatic breast cancer **New indication:** In combination with an aromatase inhibitor (AI) as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer	02/26/2018	This approval marks the third indication for Verzenio™**.** Verzenio™ was originally approved in September 2017 as the first and only cyclin-dependent kinase (CDK) 4 and 6 inhibitor for use in combination and as a single agent in metastatic breast cancer. Specifically, Verzenio™ was first approved for use: • In combination with fulvestrant for the treatment of women with HR+, HER2- advanced or metastatic breast cancer with disease progression following endocrine therapy. • As monotherapy for the treatment of adult patients with HR+, HER2- advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting. This new approval of Verzenio™ as initial therapy in combination with an AI is based on the efficacy and safety demonstrated in the MONARCH 3 Phase 3 trial, which enrolled 493 post-menopausal women with HR+, HER2- advanced breast cancer who had no prior systemic treatment for advanced disease. Verzenio™ dosed orally at 150 mg twice daily on a continuous schedule with an AI demonstrated a greater than 28-month median progression-free survival (PFS) in patients who received initial endocrine-based therapy for metastatic disease (28.2 months vs 14.8 months with placebo plus an AI). In patients with measurable disease who received Verzenio™ plus an AI (n=267), an objective response rate of 55.4% was achieved (ORR; defined as complete response plus partial response [CR + PR]), with 52.1% of patients having achieved a PR (n=139) and 3.4% having achieved a CR (n=9). Median duration of response was 27.4 months with Verzenio™ plus an AI vs 17.5 months with placebo plus an AI.

New FDA Approved Formulations

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Makena™ (hydroxyprogesterone caproate) subcutaneous auto-injector / Hologic, Inc.	Endocrine-/Metabolic agent Long acting form of natural progesterone	Prevention of preterm birth in pregnant women	02/14/2018	The new formulation was approved as a ready-to-use treatment to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous pre-term birth. Makena™ is also available as 250mg/mL strength vials for deep intramuscular (IM) injection. The IM formulation will continue to be available in single- and multi-dose vials. Both IM and SC injections must be given by a healthcare provider. They begin between weeks 16 and 21 of the pregnancy, and then continue until week 37 or the birth of the child.

New First Time Generic Drug Approval

Drug/Manufacturer	Therapeutic Class	Date	Comments
Trientine Hydrochloride Capsules 250mg / Actavis Pharma, Inc.	Antidote; Heavy metal chelator	02/07/2018	Generic for: Syprine
Sumatriptan Succinate and Naproxen Sodium Tablets 85mg (base)/ 500mg (base) / Aurobindo Pharma Limited	Antimigraine agent Sumatriptan: Selective agonist of 5-hydroxytryptamine types 1B and 1D receptors; Naproxen: NSAID	02/15/2018	Generic for: Treximet

Source: https://www.drugs.com/generic-approvals.html

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Drug/Manufacturer	Date	Indications	Comments	Impact
Patisiran / Alnylam Pharmaceuticals, Inc.	02/01/2018	Treatment For amyloidogenic transthyretin amyloidosis	FDA has accepted for filing the NDA for patisiran and granted the request for Priority Review. Patisiran is an investigational RNAi therapeutic targeting transthyretin (TTR) in development for the treatment of hereditary ATTR (hATTR) amyloidosis.	High
Omadacycline / Paratek Pharmaceuticals, Inc.	02/05/2018	Treatment for pneumonia, skin and structure infection	Paratek Pharmaceuticals, Inc. announced today that it completed the submission of two NDAs to the FDA for the Company's once-daily oral and IV formulations of its broad-spectrum investigational antibiotic, omadacycline. Omadacycline is the first in a new class of tetracycline antibiotics known an aminomethylcyclines in development for the treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI).	Moderate
Duvelisib / Verastem, Inc.	02/07/2018	Treatment for Chronic Lymphocytic Leukemia, Follicular Lymphoma, Peripheral T-cell Lymphoma, non-Hodgkin's Lymphoma	Verastem, Inc. announced it has submitted a NDA to the FDA seeking full approval for its lead product candidate duvelisib, a first-in-class oral dual inhibitor of phosphoinositide-3-kinase (PI3K)-delta and PI3K-gamma, for the treatment of relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and accelerated approval for the treatment of relapsed or refractory follicular lymphoma (FL). Duvelisib has received Fast Track Designation from the FDA for patients with CLL or peripheral T-cell lymphoma (PTCL) who have received at least one prior therapy and for patients with FL who have received at least two prior therapies. In addition, duvelisib received orphan drug designation in the United States and the European Union for patients with CLL, SLL and FL.	High High

Soruce: https://www.drugs.com/new-drug-applications.html

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Drug/Manufacturer	Date	Indications	Comments	Impact
Remoxy ER (oxycodone) / Pain Therapeutics, Inc.	02/13/2018	Treatment for pain	Pain Therapeutics, Inc. announced the resubmission to the FDA of a NDA for Remoxy ER, its lead drug candidate. Remoxy ER (oxycodone) is a long-acting, abuse-resistant, narcotic analgesic formulation in development for the treatment of moderate to severe chronic pain.	Moderate

Soruce: https://www.drugs.com/new-drug-applications.html

References:

- Drugs.com (www.drugs.com)
- Food and Drug Administration (www.fda.gov)
- Micromedex® Solutions - Truven Health Analytics (www.micromedexsolutions.com)
- Pharmacist Letter (www.pharmacistletter.com)
- P&T Community (www.ptcommunity.com)