APhA DrugInfoLine®

April 2019

Infectious Diseases

Advising on this article: Allana Sucher

April 2, 2019

Oral antibiotics for osteomyelitis and endocarditis

Key Point

Switching from I.V. to oral antibiotics, when feasible, is a strategy to decrease antimicrobial resistance. Two noninferiority studies published recently in the New England Journal of Medicine assessed the effects of oral antibiotic therapy for bone and joint infections and partial oral antibiotic treatment for endocarditis.The first study found that oral antibiotics were noninferior to I.V. antibiotics for complex orthopedic infections when given to complete the first 6 weeks of treatment. The second study showed that a switch to oral antibiotics from I.V. therapy was noninferior to I.V. antibiotics for left-sided endocarditis.

Source URL:

http://www.aphadruginfoline.com/infectious-diseases/oral-antibiotics-osteomyelitis-and-endocarditis

Focus on HIV Care

Advising on this article: Betty J. Dong

April 2, 2019

HIV treatment outcomes are better, but opportunities for improvement exist

Key Point

Antiretroviral therapy (ART) efficacy outcomes have improved in recent years, particularly with use of tenofovir/emtricitabine, integrase inhibitors, and once-daily regimens. However, more than 20% of people fail initial combination therapy at 3 years, according to results of a systematic review published in AIDS.

Source URL:

http://www.aphadruginfoline.com/focus-hiv-care/hiv-treatment-outcomes-are-better-opportunities-improvement-exist

Rheumatology

Advising on this article: Arthur A. Schuna

April 9, 2019

Rituximab and tocilizumab are effective options for people with refractory RA

Key Point

Use of rituximab (Rituxan—Genentech, Biogen) and tocilizumab (Actemra—Genentech) resulted in greater improvements in outcomes compared with abatacept (Orencia—Bristol-Myers Squibb) in people with refractory rheumatoid arthritis (RA), according to results of a population-based prospective study published in BMJ.

Source URL:

http://www.aphadruginfoline.com/rheumatology/rituximab-and-tocilizumab-are-effective-options-people-refractory-ra

Focus on Lipids Care

Advising on this article: Amber L. Briggs

April 9, 2019

Statins continue to produce vascular benefits in older adults

Key Point

Statins produce a significant reduction in major vascular events in older adults, including those older than 75 years, and older adults with established vascular disease receive greater benefits than those without vascular disease, according to a meta-analysis published in Lancet.

Source URL:

http://www.aphadruginfoline.com/focus-lipids-care/statins-continue-produce-vascular-benefits-older-adults

Focus on Anticoagulation Care

Advising on this article: Sarah Ray

April 16, 2019

VTE prophylaxis for high-risk ambulatory patients with cancer

Key Point

Use of apixaban (Eliquis—Bristol-Myers Squibb, Pfizer) as thromboprophylaxis in intermediate- to high-risk ambulatory patients receiving chemotherapy for various types of cancers reduced the risk of venous thromboembolisms (VTEs) but increased the risk of major bleeding episodes compared with placebo, and use of rivaroxaban (Xarelto—Janssen) in high-risk ambulatory patients with cancer reduced the risk of VTEs or death from a VTE during the intervention period without increasing the risk of major bleeding, according to results from two trials published in the New England Journal of Medicine.

Source URL:

http://www.aphadruginfoline.com/focus-anticoagulation-care/vte-prophylaxis-high-risk-ambulatory-patients-cancer

Focus on Asthma Care

Advising on this article: Devra K. Dang

April 16, 2019

Antimicrobial stewardship essential for hospitalized patients with asthma

Key Point

Adult patients who received antibiotics within 2 days of being hospitalized for an asthma exacerbation had extended hospital stays, higher hospital costs, higher rates of antibiotic-associated diarrhea, and a similar risk of treatment failure compared with those who did not receive antibiotics or received them later in their hospitalization, according to results of an observational study published in JAMA Internal Medicine.

Source URL:

http://www.aphadruginfoline.com/focus-asthma-care/antimicrobial-stewardship-essential-hospitalized-patients-asthma

Psychiatry

Advising on this article: M. Lynn Crismon

April 23, 2019

New analysis provides insights into preferred anxiety treatments

Key Point

Duloxetine, pregabalin (Lyrica—Pfizer), venlafaxine, and escitalopram may be the preferred treatment options for generalized anxiety disorder (GAD) based on their efficacy and safety profiles, according to results of a network meta-analysis published in Lancet.

Source URL:

http://www.aphadruginfoline.com/psychiatry/new-analysis-provides-insights-preferred-anxiety-treatments

Infectious Diseases

Advising on this article: Allana Sucher

April 23, 2019

Immediate antibiotics best approach for older adults with a UTI

Key Point

Bloodstream infections, hospital admissions, and the risk of all-cause mortality were all higher in older adults (?65 y) presenting with a UTI who were not given an antibiotic or when therapy was delayed, compared with those immediately prescribed an antibiotic, according to results of a study published in BMJ.

Source URL:

http://www.aphadruginfoline.com/infectious-diseases/immediate-antibiotics-best-approach-older-adults-uti

Supplemental Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 9, 2019	
Certolizumab pegol	FDA approved certolizumab pegol injection for treatment of adults with nonradiographic axial spondyloarthritis (nr-axSpA), with objective signs of inflammation. This is the first time FDA has approved a treatment for nr-axSpA. Nr-axSpA is a type of inflammatory arthritis that causes inflammation in the spine and other symptoms. There is no visible damage seen on x-rays, so it is referred to as nonradiographic. The drug was originally approved in 2008 and is also indicated for adult patients with Crohn’s disease, moderate to severe rheumatoid arthritis, active ankylosing spondylitis, and moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy. Its efficacy for treatment of nr-axSpA was studied in a randomized clinical trial in 317 adult patients with nr-axSpA with objective signs of inflammation, indicated by elevated C-reactive protein (CRP) levels and/or sacroiliitis on MRI. The trial measured the improvement response on the Ankylosing Spondylitis Disease Activity Score, a composite scoring system that assesses disease activity including patient-reported outcomes and CRP levels. Responses were greater for patients treated with certolizumab pegol compared with patients treated with placebo. The overall safety profile observed in the certolizumab pegol treatment group was consistent with the known safety profile of the drug. The prescribing information includes a boxed warning about the increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis, an infection that affects the lungs), and other infections. Certolizumab pegol should be discontinued if a patient develops a serious infection or sepsis. Health care providers are advised to perform testing for latent TB and, if positive, to start treatment for TB prior to starting certolizumab pegol. All patients should be monitored for

(Cimzia—UCB)

FDA approves first treatment for a type of inflammatory arthritis

active TB during treatment, even if the initial latent TB test is negative.

 The boxed warning also advises that lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor blockers such as certolizumab pegol. The agent is not indicated for use in pediatric patients.

 Certolizumab pegol must be dispensed with a patient Medication Guide that describes important information about the drug’s uses and risks.</p>

Source URL:

http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-first-treatment-type-inflammatory-arthritis

New Drug Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 9, 2019	
Testosterone undecanoate	FDA approved testosterone undecanoate, an oral testosterone capsule to treat men with certain forms of hypogonadism. These men have low testosterone levels due to specific medical conditions, such as genetic disorders like Klinefelter syndrome or tumors that have damaged the pituitary gland. Testosterone undecanoate should not be used to treat men with age-related hypogonadism, in which testosterone levels decline due to aging, even if these men have symptoms that appear to be related to low testosterone. The drug's benefits do not outweigh its risks for that use, according to FDA. Efficacy was demonstrated in a 4-month clinical trial involving 166 men with hypogonadism. Study participants initially were given 237 mg of testosterone undecanoate twice per day, and the dose was adjusted downward or upward to a maximum of 396 mg twice per day on the basis of testosterone levels. Eighty-seven percent of men treated with the drug achieved an average testosterone level within the normal range, which was the primary study endpoint. Testosterone undecanoate contains a boxed warning stating that the drug can cause blood pressure to rise, increasing the risk of heart attack, stroke, and cardiovascular death. Health care providers should consider a patient’s individual heart disease risks and ensure that blood pressure is adequately controlled before prescribing the agent. They should also periodically monitor patient blood pressure during treatment. The drug is currently one of two testosterone products that have this boxed warning. FDA is requiring all testosterone product manufacturers to conduct blood pressure postmarketing trials to more clearly address whether these products increase blood pressure. Common adverse effects, occurring in more than 2% of patients in the clinical trial, included headache, an increase in red blood cell count, a decrease in HDL-C, high blood pressure, and nausea. An increase in prostate specific antigen (PSA) was also observed. Patients should have their hematocrit, cholesterol, and PSA monitored regularly to check for

(Jatenzo—Clarus Therapeutics)

FDA approves new oral testosterone capsule for treatment of men with certain forms of hypogonadism

changes. Those with benign prostate hyperplasia should be monitored for worsening of symptoms.</p>

Source URL:

http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-new-oral-testosterone-capsule-treatment-men-certain-forms

Supplemental Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 9, 2019	
Cladribine	FDA approved cladribine tablets to treat relapsing forms of multiple sclerosis (MS) in adults, to include relapsing-remitting disease and active secondary progressive disease. Cladribine is not recommended for patients with MS who have clinically isolated syndrome. Because of its safety profile, its use is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for treatment of MS. The drug's efficacy was shown in a clinical trial in 1,326 patients with relapsing forms of MS who had least one relapse in the previous 12 months. Compared with placebo, cladribine significantly decreased the number of relapses and also reduced progression of disability. Cladribine must be dispensed with a patient Medication Guide and has a boxed warning for an increased risk of malignancy and fetal harm. It should not to be used in patients with current malignancy. In patients with prior malignancy or with increased risk of malignancy, health professionals should evaluate its benefits and risks on an individual patient basis. They should also follow standard cancer screening guidelines in patients treated with cladribine. The drug should not be used in pregnant women and in women and men of reproductive potential who do not plan to use effective contraception during treatment and for 6 months after drug therapy because of the potential for fetal harm. The drug must be stopped if the patient becomes pregnant. Other warnings include the risk of decreased lymphocyte counts, hematologic toxicity, and bone marrow suppression. Health professionals should measure a patient’s complete blood counts and lymphocyte counts before, during, and after treatment. The drug may increase the risk of infections, so health professionals should screen patients for infections and delay treatment with cladribine if necessary.

(Mavenclad—EMD Serono) **New oral treatment approved for multiple sclerosis**	The drug has been associated with graft-versus-host-disease following blood transfusions with nonirradiated blood. It may cause liver injury, and treatment should be interrupted or discontinued, as appropriate, if clinically significant liver injury is suspected. The most common adverse reactions reported in the clinical trials included upper respiratory tract infections, headache, and decreased lymphocyte counts.

Source URL:

http://www.aphadruginfoline.com/supplemental-approvals/new-oral-treatment-approved-multiple-sclerosis

Supplemental Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 9, 2019	
Ambrisentan ***(Letairis—Multiple manufacturers)*** **FDA approves multiple generics, two shared-system REMS for ambrisentan**	FDA has <a data-targettype="webpage" href="http://app.info.fda.gov/e/er?utm_campaign=FDA%20approves%20first%20generic%20versions%20of%20Letairis%20%28ambrisentan%29&utm_medium=email&utm_source=Eloqua&s=2027422842&lid=6305&elqTrackId=10101681D5209B65A27F28E06B73DDA6&elq=b5faaece8a714ef29c0b2dadf31e758d&elqaid=7391&elqat=1">approved multiple generics for ambrisentan tablets. With the approval of these first generics and their associated risk evaluation and mitigation strategy (REMS) programs, patients will now have access to additional products (brand-name and generic) and additional types of pharmacies (retail or specialty) to fill their prescriptions, according to FDA. The agency also approved two shared-system REMS programs for ambrisentan. The first, the Ambrisentan REMS (formerly the Letairis REMS), comprises the reference listed drug or brand sponsor (Letairis), as well as three abbreviated new drug applications (ANDAs, or generics). The second program, the PS-Ambrisentan REMS, currently consists of one ANDA sponsor. The PS signifies “parallel system” to assist in differentiating the programs within the market. For more information, including action items prescribers, patients, and pharmacists should complete to access these additional options, see the First Generic Drug Approvals section of FDA's website.

Source URL:

http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-multiple-generics-two-shared-system-rems-ambrisentan

Supplemental Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 9, 2019	
Aclidinium bromide/formoterol fumarate *(Duaklir—Circassia Pharmaceuticals)* **Fixed-dose LAMA/LABA combination approved for maintenance treatment of COPD**	Circassia Pharmaceuticals announced FDA approval of aclidinium bromide/formoterol fumarate for maintenance treatment of chronic obstructive pulmonary disease (COPD) under the trade name Duaklir. The agent is a fixed-dose combination of the long-acting muscarinic antagonist (LAMA) aclidinium bromide (400 mcg) and long-acting beta-agonist (LABA) formoterol fumarate (12 mcg). It is administered twice daily via the breath-actuated inhaler Pressair. Approval was based on a broad clinical database, including data from three Phase III studies, ACLIFORM, AUGMENT, and AMPLIFY. The label also includes clinical data from the Phase IV ASCENT study, which shows aclidinium therapy is effective at reducing COPD exacerbations. As a result, Duaklir is the only twice-daily LAMA/LABA in the United States with COPD exacerbation data included in its prescribing information. Circassia plans to launch Duaklir in the United States in the second half of 2019.

Source URL:

http://www.aphadruginfoline.com/supplemental-approvals/fixed-dose-lamalaba-combination-approved-maintenance-treatment-copd

Supplemental Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 9, 2019	
Tegaserod ***(Zelnorm—Sloan Pharma/US WorldMeds)*** **FDA approves reintroduction of tegaserod for IBS-C in women**	US WorldMeds announced that its subsidiary, Sloan Pharma, has received FDA approval to reintroduce tegaserod, a twice-daily oral treatment for irritable bowel syndrome with constipation (IBS-C) in women younger than 65. Tegaserod was originally approved by FDA in 2002 for treatment of IBS-C in women. It was voluntarily withdrawn from the U.S. market in 2007 because of safety concerns. The drug has remained consistently available in the United States through an expanded access program authorized by FDA and is used by patients with IBS-C in several other countries. Approval to reintroduce the agent came after a complete safety review by FDA and an FDA-assembled Gastrointestinal Drugs Advisory Committee (GIDAC). The review focused on evaluation of clinical data from 29 placebo-controlled trials and newly available sources of treatment outcome data. A positive GIDAC vote and FDA review both supported its reintroduction for appropriate patients with IBS-C. Tegaserod is the only selective serotonin-4 (5-HT4) receptor agonist approved to treat IBS-C. The drug targets the 5-HT4 receptor at multiple neurons (sensory, motor, secretory motor) and smooth muscle cells in the GI tract to induce contraction and relaxation and decrease pain signaling. In clinical trials, patients taking tegaserod saw improvement in some of the most bothersome IBS-C symptoms. In the first 4 weeks, significantly more patients treated with tegaserod than placebo-treated patients reported an improvement in their abdominal pain/discomfort and bloating. Frequency of bowel movements also increased from a median number of 3.8 per week at baseline to 6.3 per week at month one.

Source URL:

http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-reintroduction-tegaserod-ibs-c-women

Supplemental Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 9, 2019	
Palbociclib ***(Ibrance—Pfizer)*** **New indication of palbociclib approved to treat men with metastatic breast cancer**	FDA is extending the indication of palbociclib capsules in combination with specific endocrine therapies for hormone receptor–positive, human epidermal growth factor receptor 2–negative advanced or metastatic breast cancer in male patients. Palbociclib was initially approved in 2015 in combination with an aromatase inhibitor as the first hormonal-based therapy in women who have gone through menopause and in men, or with fulvestrant in patients whose disease progressed following hormonal therapy. The most common adverse effects are infections, leukopenia fatigue, nausea, stomatitis, anemia hair loss, diarrhea, and thrombocytopenia. Other common adverse effects are rash, vomiting, decreased appetite, asthenia, and fever. Health care providers are advised to monitor a patient’s blood count for neutropenia. Patients should have their blood count checked before starting palbociclib and at the beginning of each cycle, as well as on day 15 of the first two cycles and as clinically indicated. Because of the potential for genotoxicity, health care providers are advised to tell male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose. Women who are pregnant or breastfeeding should not take palbociclib because it may cause harm to a developing fetus or newborn baby.

Source URL:

http://www.aphadruginfoline.com/supplemental-approvals/new-indication-palbociclib-approved-treat-men-metastatic-breast-cancer

New Drug Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 9, 2019	
Dolutegravir and lamivudine	FDA has approved dolutegravir and lamivudine as a complete regimen for treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults with no antiretroviral treatment history and with no known or suspected substitutions associated with resistance to the individual components of the new agent. This is the first two-drug, fixed-dose, complete regimen approved for adults with HIV-1 who have never received treatment. The labeling includes a boxed warning cautioning that patients infected with both HIV and hepatitis B should receive additional treatment for their hepatitis B or consider a different drug regimen. Patients with both HIV and hepatitis B who take products containing lamivudine, an ingredient in the new combination drug, have developed hepatitis B variants associated with resistance to lamivudine. These patients may have severe liver problems, including liver failure, when they stop taking drugs containing lamivudine. Patients with both HIV and hepatitis B virus who stop using the drug should be closely monitored by their health care provider. Efficacy and safety of one tablet of dolutegravir and lamivudine taken daily were demonstrated in two identical, randomized, double-blind, controlled clinical trials in 1,433 HIV-infected adults with no prior antiretroviral treatment history. Results were similar to a drug regimen that included dolutegravir, emtricitabine, and tenofovir in reducing the amount of HIV in the blood. Treatment was considered successful if the patient maintained low levels (<50 copies/mL) of HIV RNA in their blood for at least 48 weeks. The most common adverse reactions were headache, diarrhea, nausea, insomnia, and fatigue. As there is a known risk for neural tube defects with dolutegravir, patients are advised to avoid use of the new drug at the time of conception through the first trimester of pregnancy. In May 2018, FDA released a <a href="https://www.fda.gov/Drugs/DrugSafety/

(Dovato—ViiV Healthcare)

First two-drug complete HIV regimen approved for never-treated patients

ucm608112.htm" target="">Drug Safety Communication about reported neural tube birth defects in babies born to women treated with dolutegravir.</p>

Source URL:

http://www.aphadruginfoline.com/new-drug-approvals/first-two-drug-complete-hiv-regimen-approved-never-treated-patients

New Drug Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 9, 2019	
Romosozumab-aqqg	FDA approved romosozumab-aqqg to treat osteoporosis in postmenopausal women at high risk of fracture. Women at high risk have a history of osteoporotic fracture or multiple risk factors for fracture, or have experienced treatment failure or intolerance to other osteoporosis therapies. Romosozumab-aqqg is a monoclonal antibody that blocks the effects of the protein sclerostin and works mainly by increasing new bone formation. One dose consists of two injections, one immediately following the other, given once a month by a health professional. The bone-forming effect wanes after 12 doses, so more than 12 doses should not be used. If osteoporosis therapy is needed after the 12 doses, patients should begin an osteoporosis treatment that reduces bone breakdown. Safety and efficacy of the agent were demonstrated in two clinical trials involving a total of more than 11,000 women with postmenopausal osteoporosis. In the first trial, one year of treatment with romosozumab-aqqg lowered the risk of a new vertebral fracture by 73% compared with placebo. This benefit was maintained over the second year of the trial, when the agent was followed by 1 year of denosumab (another osteoporosis therapy) compared with placebo followed by denosumab. In the second trial, one year of treatment followed by 1 year of alendronate (another osteoporosis therapy) reduced the risk of a new vertebral fracture by 50% compared with 2 years of alendronate alone. Romosozumab-aqqg followed by alendronate also reduced the risk of fractures in nonvertebral fractures compared with alendronate alone. The agent increased the risk of cardiovascular death, heart attack, and stroke in the alendronate trial but not in the placebo trial. Therefore, romosozumab-aqqg contains a boxed warning stating that it may increase the risk of heart attack, stroke, and cardiovascular death and should not be used in patients who have had a heart attack or stroke within the

(Evenity—Amgen)

FDA approves new treatment for osteoporosis in postmenopausal women at high risk of fracture

previous year.

 Health professionals should also consider whether the benefits of romosozumab-aqqg outweigh its risks in those with other risk factors for heart disease. The drug should be discontinued in any patient who experiences a heart attack or stroke during treatment. In clinical trials, common adverse effects included joint pain, headache, and injection-site reactions.

Source URL:

http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-new-treatment-osteoporosis-postmenopausal-women-high-risk-fracture

Alerts and Recalls

Generic Name (Trade Name—Company)	**Uses**/Notes
April 24, 2019	
Opioids ***(Multiple trade names—Multiple manufacturers)*** **FDA identifies harm reported from sudden discontinuation of opioid pain meds**	FDA announced that it has received reports of serious harm in patients who are physically dependent on opioid pain medications when these medications are discontinued or the dose is rapidly decreased. Rapid discontinuation can result in uncontrolled pain or withdrawal symptoms, psychological distress, and suicide. Patients may seek other sources of opioid pain medicines, which may be confused with drug-seeking for abuse, or attempt to treat their pain or withdrawal symptoms with illicit opioids, such as heroin, and other substances. Health professionals should not discontinue opioids abruptly in a patient who is physically dependent. When tapering, consider a variety of factors, including the dose, treatment duration, type of pain being treated, and a patient's physical and psychological attributes. No standard opioid tapering schedule exists that is suitable for all patients. Create a patient-specific plan to gradually taper the dose, and ensure ongoing monitoring and support, as needed, to avoid serious withdrawal symptoms, worsening of the patient’s pain, or psychological distress. FDA is tracking this safety concern as part of its ongoing monitoring of risks associated with opioid pain medications. In addition, it is requiring changes to the prescribing information that will provide expanded guidance to health professionals on how to safely decrease the dose in patients who are physically dependent on opioids. The new labeling will include additional information on other adverse effects of opioids, such as central sleep apnea and drug interactions, and on proper storage and disposal of these medications. The agency is urging patients and health professionals to report adverse effects involving opioids to the FDA MedWatch program.

Source URL:

http://www.aphadruginfoline.com/alerts-and-recalls/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-meds

Supplemental Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 24, 2019	
Pembrolizumab	FDA approved two new indications for pembrolizumab: –First-line treatment of patients with stage III non–small cell lung cancer (NSCLC) who are not candidates for surgical resection or definitive chemoradiation for metastatic NSCLC. Patients’ tumors must have no EGFR or ALK genomic aberrations and express PD-L1 (Tumor Proportion Score [TPS] ≥ 1%), as determined by an FDA-approved test. –With axitinib for first-line treatment of patients with advanced renal cell carcinoma (RCC). Approval for stage III or IV NSCLC was based on KEYNOTE?042, a randomized, multicenter, open-label, active-controlled trial conducted in 1,274 patients with stage III or IV NSCLC who had not received prior systemic treatment for metastatic NSCLC and whose tumors expressed PD-L1 (TPS ≥ 1%). The trial demonstrated statistically significant OS improvements for those randomized to pembrolizumab compared with chemotherapy in all three populations. The recommended dosage for NSCLC is 200 mg as an I.V. infusion over 30 minutes every 3 weeks. The most common adverse reactions are fatigue, decreased appetite, dyspnea, cough, rash, constipation, diarrhea, nausea, hypothyroidism, pneumonia, pyrexia, and weight loss. Approval for RCC was based on KEYNOTE?426, a randomized, multicenter, open-label trial conducted in 861 patients who had not received systemic therapy for advanced RCC. Patients were enrolled regardless of PD-L1 tumor expression status and were randomly allocated to receive either pembrolizumab 200 mg intravenously every 3 weeks in combination with axitinib 5 mg orally twice daily, or sunitinib 50 mg orally once daily for 4 weeks and then off treatment for 2 weeks. Treatment continued until confirmed disease progression or unacceptable toxicity. Pembrolizumab was received for maximum of 24 months. The recommended dosage for this indication is pembrolizumab 200 mg every

(Keytruda—Merck)

FDA approves two new indications for pembrolizumab

3 weeks with axitinib 5 mg orally twice daily.

 The most common adverse reactions for pembrolizumab plus axitinib are diarrhea, fatigue/asthenia, hypertension, hypothyroidism, decreased appetite, hepatotoxicity, palmar-plantar erythrodysesthesia, nausea, stomatitis/mucosal inflammation, dysphonia, rash, cough, and constipation.

Source URL:

http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-two-new-indications-pembrolizumab

New Drug Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 24, 2019	
Erdafitinib	FDA granted accelerated approval to erdafitinib for treatment of adult patients with locally advanced or metastatic bladder cancer that has a FGFR3 or FGFR2 genetic alteration, and that has progressed during or following prior platinum-containing chemotherapy. An FDA-approved companion diagnostic device must be used to select patients for treatment. Bladder cancer is the sixth most common cancer in the United States. Transitional cell carcinoma, also called urothelial carcinoma, is the most common type. Bladder cancers are associated with genetic mutations that are present in the patient's bladder or entire urothelium. Fibroblast growth factor (FGFR) alterations are present in approximately one in five patients with recurrent and refractory bladder cancer. Efficacy of erdafitinib was studied in a clinical trial that included 87 patients with locally advanced or metastatic bladder cancer, with FGFR3 or FGFR2 genetic alterations, that had progressed following treatment with chemotherapy. The overall response rate in these patients was 32.2%, with 2.3% having a complete response and almost 30% having a partial response. The response lasted for an average of approximately 5.5 months. About a quarter of patients in the study were previously treated with anti PD-L1/PD-1 therapy, which is a standard treatment for patients with locally advanced or metastatic bladder cancer. Responses to erdafitinib were seen in patients who had previously not responded to anti PD-L1/PD-1 therapy. Common adverse effects are increased phosphate level, mouth sores, fatigue, change in kidney function, diarrhea, dry mouth, nails separating from the bed or poor formation of the nail, change in liver function, low sodium levels, decreased appetite, change in sense of taste, anemia, dry skin, dry eyes, and hair loss. Other adverse effects are redness, swelling, peeling or tenderness on the hands or feet, constipation, stomach pain, nausea, and muscle pain. Erdafitinib may cause serious eye problems, including inflamed eyes, inflamed cornea, and disorders of the retina. Patients are advised to have eye examinations intermittently and

(Balversa—Janssen)

FDA approves first targeted therapy for metastatic bladder cancer

to tell their health professional right away if they develop blurred vision, loss of vision, or other visual changes. Health professionals are advised to check patients’ blood phosphate level between 14 and 21 days after starting treatment and monthly, and to increase the dose of erdafitinib in patients whose serum phosphate is below the target level. Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment and for 1 month after the last dose. Pregnancy testing is recommended for females of reproductive potential before initiating treatment. Women who are pregnant or breastfeeding should not take erdafitinib because it may cause harm to a developing fetus or newborn baby.

Source URL:

http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-first-targeted-therapy-metastatic-bladder-cancer

Alerts and Recalls

Generic Name (Trade Name—Company)	**Uses**/Notes
April 24, 2019	
No generic name ***(Aphrodisiac capsules—SD Import)*** **Dietary supplement containing undeclared sildenafil poses health risk**	SD Import is voluntarily recalling all lots of aphrodisiac capsules to the consumer level. An FDA analysis found the product is tainted with sildenafil, an FDA-approved active pharmaceutical ingredient (API) used to treat erectile dysfunction. Presence of the sildenafil renders the capsules an unapproved drug for which safety and efficacy have not been established and, therefore, subject to recall. Consumers with diabetes, hypertension, high cholesterol, or heart disease often take nitrates; consumption of undeclared sildenafil along with nitrates could result in a drop in blood pressure that is life-threatening and could result in serious adverse health consequences. Aphrodisiac capsules are marketed as a dietary supplement for men for sexual enhancement and are packaged in a cardboard box with 12 plastic packs in a box (UPC Code 644118128135). The product was distributed nationwide to retail stores and a variety of online websites. SD Imports is notifying its distributors and customers by e-mail and arranging for return of all recalled products. The company indicated that, to date, it has not received any reports of adverse events related to this recall.

Source URL:

http://www.aphadruginfoline.com/alerts-and-recalls/dietary-supplement-containing-undeclared-sildenafil-poses-health-risk

Supplemental Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 24, 2019	
Generic naloxone	FDA has granted final approval of the first generic naloxone hydrochloride nasal spray, commonly known as Narcan, a life-saving medication that can stop or reverse the effects of an opioid overdose. The agency is also planning new steps to prioritize the review of additional generic drug applications for products intended to treat opioid overdose, along with the previously announced action to help facilitate an OTC naloxone product. Though the approval is the first generic naloxone nasal spray for use in a community setting by individuals without medical training, generic injectable naloxone products have been available for years for use in a health care setting. FDA also has previously approved a brand-name naloxone nasal spray and an auto-injector for use by those without medical training. In a press announcement, FDA said that while business and other considerations may affect how quickly this product becomes available, the approval is an important step for the agency as it works toward expanding access to this live-saving drug. FDA also held a two-day advisory committee meeting in December to solicit input and advice on strategies to increase the availability of naloxone products intended for use in the community. Naloxone nasal spray does not require assembly and delivers a consistent, measured dose when used as directed. This product can be used for adults or children and is easily administered by anyone, even those without medical training. The drug is sprayed into one nostril while the patient is lying on his or her back and can be repeated if necessary. Use of naloxone nasal spray in patients who are opioid-dependent may result in severe opioid withdrawal characterized by body aches, diarrhea, increased heart rate, fever, runny nose, sneezing, goose bumps, sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, shivering or trembling,

(Narcan generic—Teva)

FDA approves first generic naloxone nasal spray to treat opioid overdose

abdominal cramps, weakness, and increased blood pressure.</p>

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http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-first-generic-naloxone-nasal-spray-treat-opioid-overdose

Alerts and Recalls

Generic Name (Trade Name—Company)	**Uses**/Notes
April 24, 2019	
Fentanyl transdermal patches ***(Fentanyl Transdermal System 12—Alvogen/3M Drug Delivery Systems)*** **Two lots of fentanyl transdermal patches recalled due to product mislabeling**	Alvogen is voluntarily recalling two lots (#180060 and #180073) of 12-mcg/h fentanyl transdermal patches because a small number of cartons were found to contain 50-mcg/h patches. The 50-mcg/h patches that were included in cartons labeled 12 mcg/h are individually labeled as 50 mcg/h. The transdermal system is manufactured by 3M Drug Delivery Systems, St. Paul, MN. Application of a 50-mcg/h patch instead of a prescribed 12-mcg/h patch could result in serious, life-threatening, or fatal respiratory depression. Groups at potential increased risk could include first-time recipients of such patches, children, and older adults. The product is indicated for management of pain in opioid-tolerant patients and is packaged in primary cartons of five individually wrapped and labeled pouches. Alvogen is notifying its distributors and direct customers by certified letter and is arranging for return and replacement of all recalled products. Pharmacies should not dispense any product subject to this recall. Patients who have the product should immediately remove any patch currently in use, contact their health care provider, and return the unused product to point of purchase for replacement. To date, Alvogen has not received any reports of adverse events related to this recall.

Source URL:

http://www.aphadruginfoline.com/alerts-and-recalls/two-lots-fentanyl-transdermal-patches-recalled-due-product-mislabeling

New Drug Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
April 25, 2019	
Risankizumab-rzaa ***(Skyrizi—Boehringer/AbbVie)*** **IL-23 inhibitor approved for moderate to severe plaque psoriasis**	FDA approved risankizumab-rzaa, an interleukin-23 (IL-23) inhibitor, to treat moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. In clinical trials, risankizumab produced high rates of durable skin clearance, with most participants (82% and 81%) achieving a 90% skin clearance (PASI 90) at 1 year, and the majority (56% and 60%) achieving complete skin clearance (PASI 100). The recommended dose is 150 mg administered by two S.C. injections every 12 weeks following two initiation doses at weeks 0 and 4. The drug can be administered in the office or by self-injection after training. The most common adverse events associated with risankizumab are upper respiratory infections, headache, fatigue, injection-site reactions, and tinea infections. The drug requires an initial evaluation for tuberculosis (TB) prior to starting treatment, and patients are instructed to report signs and symptoms of infection.

Source URL:

http://www.aphadruginfoline.com/new-drug-approvals/il-23-inhibitor-approved-moderate-severe-plaque-psoriasis

Alerts and Recalls

Generic Name (Trade Name—Company)	**Uses**/Notes
April 25, 2019	
Flibanserin ***(Addyi—Sprout Pharmaceuticals)*** **Labeling changes will loosen alcohol restrictions for flibanserin**	On April 11, 2019, FDA announced that changes must be made to the labeling for flibanserin to clarify that there is still a concern about consuming alcohol close in time to taking the drug, but that alcohol does not have to be avoided completely. Specifically, the boxed warning, contraindication, warnings and precautions, and adverse reactions sections of labeling are being updated to reflect that women should discontinue drinking alcohol at least 2 hours before taking flibanserin at bedtime or to skip the flibanserin dose that evening. Women should not consume alcohol at least until the morning after taking flibanserin at bedtime. FDA is ordering this safety labeling change because the agency was not able to reach an agreement with the manufacturer, Sprout Pharmaceuticals. The company was continuing to request removal of the boxed warning and contraindication about alcohol completely from the product labeling. FDA determined, based on a careful review of available data, that to protect public health, removing this important safety information was not acceptable. The agency's decision to order modifications to the warnings about flibanserin and alcohol, instead of removing the boxed warning and contraindication completely, was based on two sets of postmarket research studies. Flibanserin is a serotonin 1A receptor agonist and a serotonin 2A receptor antagonist, but the mechanism by which the drug improves sexual desire and related distress is not known. The drug is taken once daily at bedtime to help decrease the risk of adverse events from possible hypotension, syncope, and CNS depression (such as sleepiness and sedation). Patients should stop treatment after 8 weeks if they do not have an improvement in sexual desire and associated distress. The drug's most common adverse reactions are dizziness, sleepiness, nausea, fatigue, insomnia, and dry mouth.

Source URL:

http://www.aphadruginfoline.com/alerts-and-recalls/labeling-changes-will-loosen-alcohol-restrictions-flibanserin