
A^{PhA} **DrugInfoLine[®]**

October 2018

[Focus on Diabetes Care](#)

Advising on this article: Charles D. Ponte

October 1, 2018

Some older adults with type 2 diabetes may be overtreated

Key Point

Approximately one-quarter of older adults (>75 y) with type 2 diabetes were treated with medications associated with a high risk of hypoglycemia to achieve tight glycemic control, according to an observational analysis of a large U.S. outpatient cohort published in the Journal of the American Geriatrics Society.

Source URL:

<http://www.aphadruonline.com/focus-diabetes-care/some-older-adults-type-2-diabetes-may-be-overtreated>

[Cardiology](#)

Advising on this article: Eric MacLaughlin

October 1, 2018

Three-drug, low-dose, fixed-combination product is effective for BP control

Key Point

A three-drug, low-dose, fixed-combination dosage form resulted in better blood pressure (BP) control at 6 months compared with usual care in patients with mild to moderate hypertension, according to results of a randomized trial published in JAMA.

Source URL:

<http://www.aphadruginfoline.com/cardiology/three-drug-low-dose-fixed-combination-product-effective-bp-control>

[Infectious Diseases](#)

Advising on this article: Allana Sucher

October 9, 2018

Patients labeled as penicillin-allergic and MRSA and C. difficile infections

Key Point

The risk of methicillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* infections was higher in patients who reported a penicillin allergy compared with those who did not, according to results of an observational study published in BMJ. The risks of developing MRSA and *C. difficile* were reportedly mediated by use of alternative broad-spectrum non-β-lactam antibiotics.

Source URL:

<http://www.aphadruginfoline.com/infectious-diseases/patients-labeled-penicillin-allergic-and-mrsa-and-c-difficile-infections>

[Gastroenterology](#)

Advising on this article: C. Wayne Weart

October 9, 2018

Glutamine may be an option for postinfectious irritable bowel syndrome

Key Point

Use of glutamine supplementation in patients with postinfectious diarrhea-predominant irritable bowel syndrome (IBS-D) resulted in greater improvements in gastrointestinal (GI) symptoms and changes in daily bowel movement frequency, stool form, and intestinal permeability compared with placebo, according to results of a small study published in *Gut*.

Source URL:

<http://www.aphadruginfoline.com/gastroenterology/glutamine-may-be-option-postinfectious-irritable-bowel-syndrome>

[Infectious Diseases](#)

Advising on this article: Allana Sucher

October 16, 2018

Extended-pulsed fidaxomicin a good option for *C. difficile* infections

Key Point

Use of extended-pulsed fidaxomicin (Dificid–Merck) was superior to standard-dose vancomycin when given to older patients with *Clostridium difficile* infections with respect to sustained clinical cure rates 30 days after the end of treatment, according to results of a trial published in *Lancet Infectious Diseases*.

Source URL:

<http://www.aphadruinfo.com/infectious-diseases/extended-pulsed-fidaxomicin-good-option-c-difficile-infections>

[Focus on HIV Care](#)

Advising on this article: Betty J. Dong

October 16, 2018

Resistance to HIV medications rare during preexposure prophylaxis

Key Point

Primary drug resistance to either tenofovir disoproxil fumarate (TDF) and/or emtricitabine (FTC, Truvada—Gilead) was rare in people who acquired HIV infection while enrolled in a preexposure prophylaxis (PrEP) trial, according to an analysis of data published in AIDS.

Source URL:

<http://www.aphadruginfoline.com/focus-hiv-care/resistance-hiv-medications-rare-during-preexposure-prophylaxis>

[Pharmacogenomics Corner](#)

Advising on this article: Mary W. Roederer

October 23, 2018

Both clinic and in-home pharmacogenomic testing are valuable to patients

Key Point

People who had either a clinic-based or an in-home pharmacogenomic test were satisfied with the testing experience, found the results to be helpful, and felt they had a good understanding of the results, according to results of a survey published in *Pharmacogenomics*, and some people were concerned with privacy and discrimination issues.

Source URL:

<http://www.aphadruginfoline.com/pharmacogenomics-corner/both-clinic-and-home-pharmacogenomic-testing-are-valuable-patients>

Cardiology

Advising on this article: Eric MacLaughlin

October 29, 2018

Aspirin may not be a good option for primary prevention in diabetes

Key Point

The benefits of low-dose aspirin in preventing serious vascular events in patients with diabetes and no evidence of cardiovascular (CV) disease did not outweigh the risk of major bleeding, according to results of the ASCEND trial published in the New England Journal of Medicine.

Source URL:

<http://www.aphadruonline.com/cardiology/aspirin-may-not-be-good-option-primary-prevention-diabetes>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

October 1, 2018

Cemiplimab-rwlc

(Libtayo—Regeneron Pharmaceuticals)

FDA approves first treatment for advanced form of the second most common skin cancer

Uses/Notes

[FDA approved](#) cemiplimab-rwlc injection for I.V. use for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation. This is the first FDA approval of a drug specifically for advanced CSCC.

By blocking the PD-1 pathway, cemiplimab-rwlc may help the body's immune system fight the cancer cells.

Safety and efficacy of cemiplimab-rwlc was studied in two open-label clinical trials. Results showed that 47.2% percent of all patients treated with the agent had their tumors shrink or disappear. The majority of these patients had ongoing responses at the time of data analysis.

Common adverse effects of cemiplimab-rwlc include fatigue, rash, and diarrhea. The agent must be dispensed with a patient Medication Guide that describes uses of the drug and its serious warnings.

Serious adverse reactions include the risk of immune-mediated adverse reactions such as pneumonitis, colitis, hepatitis, endocrinopathies, and dermatologic and kidney problems. Patients should also be monitored for infusion-related reactions.

Because the agent can cause harm to a developing fetus, women should be advised of the potential risk to the fetus and to use effective contraception.

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-first-treatment-advanced-form-second-most-comm-on-skin-cancer>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

October 1, 2018

Amikacin liposome inhalation suspension

Uses/Notes

[FDA approved](#) amikacin liposome inhalation suspension to treat lung disease caused by a group of bacteria, Mycobacterium avium complex (MAC), in a limited population of patients with the disease who do not respond to conventional treatment. The drug is an inhaled treatment taken through a nebulizer.

MAC is a type of nontuberculous mycobacteria (NTM) commonly found in water and soil. Symptoms of disease in patients with MAC include persistent cough, fatigue, weight loss, night sweats, and occasionally, shortness of breath and coughing up of blood.

It is the first drug to be approved under the [Limited Population Pathway for Antibacterial and Antifungal Drugs](#), or LPAD pathway, established by Congress under the [21st Century Cures Act](#) to advance development and approval of antibacterial and antifungal drugs to treat serious or life-threatening infections in a limited population of patients with unmet need. Approval under the LPAD pathway may be supported by a streamlined clinical development program. These programs may involve smaller, shorter, or fewer clinical trials. As required for drugs approved under the LPAD pathway, the labeling includes certain statements to convey that the drug has been shown to be safe and effective only for use in a limited population.

Approval was based on achieving three consecutive negative monthly sputum cultures by month six of treatment. FDA requires the sponsor to conduct an additional postmarketing study to describe the drug's clinical benefits.

Safety and efficacy were demonstrated in a randomized, controlled clinical trial in which patients were assigned to one of two treatment groups: one group receiving amikacin plus a background multidrug antibacterial regimen, and the other group receiving a background multidrug antibacterial regimen alone.

By the sixth month of treatment, 29% percent of patients treated with amikacin had no growth of mycobacteria in their sputum cultures for three consecutive months,

(Arikayce—Insmed)

New antibacterial drug treats serious lung disease caused by *Mycobacterium avium* complex

compared with 9% of patients who were not treated with amikacin.

The prescribing information includes a boxed warning about the increased risk of respiratory conditions. Other common adverse effects are difficulty speaking, cough, damaged hearing, upper airway irritation, musculoskeletal pain, fatigue, diarrhea, and nausea.

Source URL:

<http://www.aphadruinfo.com/new-drug-approvals/new-antibacterial-drug-treats-serious-lung-disease-caused-mycobacterium-avium>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

October 1, 2018

Galcanezumab-gnlm

(*Emgality—Eli Lilly*)

New drug approved for preventive treatment of migraine in adults

Uses/Notes

[FDA has approved](#) galcanezumab-gnlm, a calcitonin gene-related peptide (CGRP) antagonist, as a once-monthly, self-administered, S.C. 120-mg injection for preventive treatment of migraine in adults.

Efficacy and safety of galcanezumab-gnlm were demonstrated in two Phase III clinical trials (EVOLVE-1 and EVOLVE-2) in patients with episodic migraine and one Phase III clinical trial (REGAIN) in patients with chronic migraine.

Safety was evaluated in three clinical trials that included more than 2,500 patients. Hypersensitivity reactions (e.g., rash, urticaria and dyspnea) have been reported in clinical studies, can occur days after administration, and may be prolonged. The most common adverse effects were injection-site reactions.

The recommended dose for galcanezumab-gnlm is 240 mg (two consecutive S.C. injections of 120 mg each), once as a loading dose, followed by monthly doses of 120 mg injected subcutaneously.

Galcanezumab-gnlm is contraindicated in patients with serious hypersensitivity to galcanezumab-gnlm or to any of the excipients.

Patients with commercial insurance are candidates to receive galcanezumab-gnlm for up to 12 months free as part of Lilly's patient support program.

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/new-drug-approved-preventive-treatment-migraine-adults>

[Supplemental Approvals](#)

Generic Name (Trade Name—Company)

October 2, 2018

Testosterone enanthate

(Xyosted—Antares Pharma)

FDA approves first S.C. testosterone enanthate injection for once-weekly, at-home self-administration

Uses/Notes

[Antares Pharma announced](#) FDA approval of testosterone enanthate, the first testosterone replacement therapy for conditions associated with a deficiency or absence of endogenous testosterone in adult males.

The product is self-administered subcutaneously once weekly at home with an easy-to-use, single-dose, disposable QuickShot auto injector. It comes in three dosage strengths: 50 mg, 75 mg, and 100 mg.

In Phase III clinical trials, the product was shown to produce physiologically normal levels of testosterone with a narrow peak-to-trough ratio. According to the principal investigator, the S.C. dosing removes transfer concerns commonly associated with gels and potentially reduces the need for in-office injection procedures that may require more frequent patient visits.

The product can cause blood pressure elevations that can increase the risk for major adverse cardiovascular events (MACE), including nonfatal myocardial infarction, nonfatal stroke and cardiovascular death, with greater risk for MACE in patients with cardiovascular risk factors or established cardiovascular disease.

The most commonly reported adverse reactions in clinical trials were hematocrit increases, hypertension, prostate-specific antigen increases, injection-site bruising, and headache.

Recommended dosage is 100–400 mg every 4 weeks.

Source URL:

<http://www.aphadruginfo.com/supplemental-approvals/fda-approves-first-sc-testosterone-enthate-injection-once-weekly-home-self>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

October 2, 2018

Sarecycline

(Seysara—Almiral)

New oral antibiotic targets moderate to severe acne

Uses/Notes

[Amirall announced](#) FDA approval of sarecycline, an innovative first-in-class tetracycline-derived oral antibiotic for treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients aged 9 years and older.

Sarecycline is an oral tablet that is taken once daily with or without food. It has proven to significantly reduce inflammatory lesions as early as 3 weeks after start of treatment and is generally safe and well tolerated.

Safety of the product was established in two 12-week multicenter, randomized, double-blind, placebo-controlled studies. Efficacy was assessed in 2,002 participants aged 9 years and older. Efficacy of sarecycline beyond 12 weeks and safety beyond 12 months have not been established.

Sarecycline has not been evaluated for treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, patients should use sarecycline only as indicated. The product is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines.

Use during tooth development may cause permanent discoloration of the teeth. If *Clostridium difficile*-associated diarrhea (antibiotic-associated colitis) or intracranial hypertension occurs, use should be discontinued. Central nervous system adverse effects, including light-headedness, dizziness, or vertigo, have been reported with tetracycline use. The most common adverse reaction is nausea.

Sarecycline is expected to be launched in January 2019.

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/new-oral-antibiotic-targets-moderate-severe-acne>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

October 4, 2018

Omadacycline

Uses/Notes

[Paratek announced](#) FDA approval of omadacycline 100 mg for injection/150 mg tablets for treatment of community-acquired bacterial pneumonia (CABP) and acute skin and skin structure infections (ABSSSI) in adults.

Omadacycline, a modernized tetracycline, is a once-daily I.V. and oral antibiotic that targets a spectrum of bacteria, including Gram-positive, Gram-negative, atypicals, and drug-resistant strains.

Approval was supported by multiple clinical trials involving nearly 2,000 adult patients.

Warnings and precautions include the following:

Use during tooth development (last half of pregnancy, infancy, and childhood to age 8) may cause permanent discoloration of the teeth (yellow-gray-brown) and enamel hypoplasia.

Use during the second and third trimester of pregnancy, infancy and childhood up to age 8 years may cause reversible inhibition of bone growth.

Omadacycline is structurally similar to other tetracycline-class antibacterial drugs and is contraindicated in patients with known hypersensitivity to tetracycline-class antibacterial drugs.

Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents and may range in severity from mild diarrhea to fatal colitis.

The most common adverse reactions (incidence ≥2%) in clinical trials were nausea, vomiting, infusion-site reactions, alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyl transferase increased, hypertension, headache, diarrhea, insomnia, and constipation.

The drug is expected to become available in the first quarter of 2019.

(Nuzyra—Paratek)

FDA approves once-daily I.V. and oral antibiotic for treatment of CABP and ABSSI

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-once-daily-iv-and-oral-antibiotic-treatment-cabp-and-abssi>

Alerts and Recalls

Generic Name (Trade Name—Company)

October 4, 2018

No generic name

(NeoRelief for Muscle Cramping and Restlessness Topical Gel—BioLyte Laboratories/King Bio Inc.)

Topical gel recalled due to possible microbial contamination

Uses/Notes

BioLyte Laboratories is voluntarily [recalling](#) lot numbers 1138, 1139, 1146, and 1160 of NeoRelief for Muscle Cramping and Restlessness Topical Gel to the retail and consumer level.

King Bio Inc., a manufacturer of some of the active ingredients in this product, has been found to have some water contamination issues that could have affected this product. King Bio has issued a recall of these active ingredients in BioLyte's lot specific product.

Administration or use of drug products with microbial contamination could result in increased infections that may require medical intervention or that could be life threatening to certain individuals.

Lot Number	Expiry	UPC	Size	Package type
1138	1/31/2020	35836800 2021	2 oz	white airless pump bottle
1139	1/31/2020	35836800 2021	2 oz	white airless pump bottle
1146	3/29/2020	35836800 2045	4 ml	4" x 2" mylar foil pack
1160	10/10/201 9	35836800 2021	2 oz	white airless pump bottle

BioLyte Laboratories is notifying its retail partners, distributors, and customers by letter and is arranging for return and replacement of the recalled product.

To date, there have been no reports of illness or injury due to use of this product.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/topical-gel-recalled-due-possible-microbial-contamination>

[Supplemental Approvals](#)

Generic Name (Trade Name—Company)

October 9, 2018

Human papillomavirus 9-valent vaccine, recombinant

Uses/Notes

[FDA approved](#) a supplemental application for human papillomavirus (HPV) 9-valent vaccine, recombinant (Gardasil 9), expanding the approved use to include women and men aged 27 through 45 years. Gardasil 9 prevents certain cancers and diseases caused by the nine HPV types covered by the vaccine.

Gardasil, a vaccine approved by FDA in 2006 to prevent certain cancers and diseases caused by four HPV types, is no longer distributed in the United States. In 2014, FDA approved Gardasil 9, which covers the same four HPV types as Gardasil, as well as an additional five HPV types. Gardasil 9 was approved for use in males and females aged 9 through 26 years.

Effectiveness of Gardasil is relevant to Gardasil 9 since the vaccines are manufactured similarly and cover four of the same HPV types. In a study in approximately 3,200 women aged 27 through 45 who were followed for an average of 3.5 years, Gardasil was 88% effective in preventing a combined endpoint of persistent infection, genital warts, vulvar and vaginal precancerous lesions, cervical precancerous lesions, and cervical cancer related to HPV types covered by the vaccine.

FDA's approval of Gardasil 9 in women aged 27 through 45 is based on these results and new data on long-term follow-up from this study.

Effectiveness of Gardasil 9 in men aged 27 through 45 is inferred from the data described above in women aged 27 through 45, as well as efficacy data from Gardasil in younger men (aged 16–26 y) and immunogenicity data from a clinical trial in which 150 men, aged 27 through 45, received a three-dose regimen of Gardasil over 6 months.

Safety of Gardasil 9 was evaluated in approximately 13,000 males and females. The most commonly reported adverse reactions were injection-site pain, swelling, redness, and headaches.

FDA granted the Gardasil 9 application priority review status. This program facilitates and expedites the review

(Gardasil 9—Merck, Sharp & Dohme)

of medical products that address a serious or life-threatening condition.

FDA approves expanded use of Gardasil 9 to include individuals aged 27 through 45 years

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-expanded-use-gardasil-9-include-individuals-aged-27-through-45>

[Supplemental Approvals](#)

Generic Name (Trade Name—Company)

October 18, 2018

Emicizumab-kxwh injection

(*Hemlibra*—Genentech)

FDA approves emicizumab-kxwh for hemophilia A with or without Factor VIII inhibitors

Uses/Notes

FDA approved [emicizumab-kxwh injection](#) to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients (aged newborn and older) with hemophilia A (congenital factor VIII deficiency) with or without factor VIII (FVIII) inhibitors.

The agent was first approved in 2017 for patients with hemophilia A with FVIII inhibitors.

The current approval was based on two clinical trials: HAVEN 3 (NCT02847637) and HAVEN 4 (NCT03020160). This approval expanded the indication for patients with hemophilia A without FVIII inhibitors and provided for new dosing regimens for patients with and without FVIII inhibitors.

The prescribing information includes a warning that thrombotic microangiopathy and thrombotic events were reported when on average a cumulative amount of greater than 100 U/kg/24 hours of activated prothrombin complex concentrate (aPCC) was administered for 24 hours or more to patients receiving prophylaxis with emicizumab-kxwh. Patients should be monitored for the development of thrombotic microangiopathy and thrombotic events if aPCC is administered. aPCC should be discontinued and emicizumab-kxwh dosing should be suspended if there is evidence of thrombotic microangiopathy or an acute thrombotic event.

The most common adverse reactions reported (incidence ≥10%) were injection-site reactions, headache, and arthralgia.

The recommended loading dose is 3 mg/kg by S.C. injection once weekly for the first 4 weeks for all approved prophylactic dosing regimens. In addition to the already approved weekly dose of 1.5 mg/kg, the new maintenance dosing regimens include 3 mg/kg by S.C. injection once every 2 weeks and 6 mg/kg by S.C. injection every 4 weeks.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-emicizumab-kxwh-hemophilia-or-without-factor>

-viii-inhibitors

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

October 18, 2018

Inotersen

(Tegsedi—Akcea Therapeutics and Ionis Pharma)

Agent targets polyneuropathy of hATTR in adults

Uses/Notes

Akcea Therapeutics and Ionis Pharma [announced](#) FDA approval of inotersen for treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR) in adults. It reduces the production of transthyretin (TTR) protein through a once-weekly S.C. injection. In hATTR amyloidosis, TTR protein misfolds and accumulates as amyloid deposits throughout the body.

FDA's approval of inotersen was based on results from the Phase III NEURO-TTR study in patients with hATTR amyloidosis with symptoms of polyneuropathy.

Results demonstrated that patients treated with inotersen experienced significant benefit compared with patients treated with placebo across both coprimary endpoints: the Norfolk Quality of Life Questionnaire–Diabetic Neuropathy and modified Neuropathy Impairment Score +7, a measure of neuropathic disease progression.

Inotersen is associated with risk of thrombocytopenia and glomerulonephritis. Enhanced monitoring is required to support early detection and management of these identified risks. For full prescribing information, including a boxed warning, please visit www.TEGSEDI.com. Inotersen is being marketed with a Risk Evaluation and Mitigation Strategy (REMS).

The most common adverse effects include injection-site reactions (such as redness or pain at the injection site), nausea, headache, tiredness, low platelet counts, and fever.

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/agent-targets-polyneuropathy-hattr-adults>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

October 24, 2018

Baloxavir marboxil

(Xofluza—Shionogi & Co., Ltd.)

FDA approves new antiviral drug to treat influenza

Uses/Notes

[FDA has approved](#) a new antiviral drug, baloxavir marboxil, to treat acute uncomplicated influenza (flu) in patients aged 12 years and older who have been symptomatic for no more than 48 hours.

According to FDA Commissioner Scott Gottlieb, MD, the polymerase acidic (PA) endonuclease inhibitor is the first new antiviral flu treatment with a novel mechanism of action approved by FDA in nearly 20 years.

Safety and efficacy of baloxavir marboxil taken as a single oral dose was demonstrated in two randomized controlled clinical trials of 1,832 patients in which participants were assigned to receive either baloxavir marboxil, a placebo, or another antiviral flu treatment within 48 hours of experiencing flu symptoms.

In both trials, patients treated with baloxavir marboxil had a shorter time to alleviation of symptoms compared with patients who took the placebo. In the second trial, there was no difference in the time to alleviation of symptoms between participants who received baloxavir marboxil and those who received the other flu treatment.

Within 48 hours of symptom onset, patients weighing 40 kg to less than 80 kg take a single oral dose of 40 mg, and patients weighing at least 80 kg take a single oral dose of 80 mg, with or without food. Avoid coadministration with dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives, antacids, or oral supplements (e.g., calcium, iron, magnesium, selenium, or zinc).

Common adverse reactions in clinical trials were diarrhea and bronchitis.

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-new-antiviral-drug-treat-influenza>

[Supplemental Approvals](#)

Generic Name (Trade Name—Company)

October 24, 2018

Rituximab

(Rituxan—Genentech)

Label update approved for two rare forms of vasculitis

Uses/Notes

[Genentech announced](#) an update to the rituximab label to include information on follow-up treatment of adult patients with granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) who have achieved disease control with induction treatment.

GPA and MPA are two types of antineutrophil cytoplasmic antibody–associated vasculitis, or inflammation of the blood vessels, that largely affects the small blood vessels of the kidneys, lungs, and a variety of other organs.

The label update was based on data from a Roche-supported study by the French Vasculitis Study Group showing that treatment with the rituximab regimen (rituximab and glucocorticoids) resulted in fewer major relapses by month 28 compared with treatment with azathioprine. The observed safety profile was consistent with that previously observed in this patient population.

In combination with glucocorticoids, rituximab was approved by FDA in 2011 for adult patients with GPA and MPA with the precaution that limited data were available on the safety and efficacy of subsequent courses of rituximab in patients with GPA and MPA, and that the safety and efficacy of retreatment with rituximab had not been established. As part of this label update, the precaution has been removed from the rituximab prescribing information.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/label-update-approved-two-rare-forms-vasculitis>

Supplemental Approvals

Generic Name (Trade Name—Company)

October 25, 2018

Dupilumab

(Dupixent—Regeneron, Sanofi Genzyme)

Dupilumab now approved for treatment of moderate to severe asthma

Uses/Notes

[Dupilumab](#) gained FDA approval as add-on maintenance therapy for patients with moderate to severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma.

Dupilumab inhibits the overactive signaling of interleukin-4 (IL-4) and interleukin-13 (IL-13), two key proteins that contribute to the type 2 inflammation that may underlie moderate to severe asthma. This effect is associated with the reduction of inflammatory biomarkers, including fractional exhaled nitric oxide, immunoglobulin E, and eotaxin-3.

For people with asthma, dupilumab comes in two doses (200 mg and 300 mg) given every other week at different injection sites after an initial loading dose.

Approval for the indication was based on a pivotal trial program that evaluated 2,888 adult and adolescent patients with moderate to severe asthma in three randomized, placebo-controlled, multicenter trials for 6 months to 1 year (24 to 52 weeks).

The agent comes in a pre-filled syringe and is intended for subcutaneous injection under the guidance of a health care provider. It can be given in a clinic or, for convenience, at home by self-administration after training by a health professional.

Dupilumab was previously approved for treatment of adults with moderate to severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies, or when those therapies are not advisable.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/dupilumab-now-approved-treatment-moderate-severe-asthma>

[Supplemental Approvals](#)

Generic Name (Trade Name—Company)

October 25, 2018

Rivaroxaban

(Xarelto—Janssen)

FDA approves new indication in twice-daily dose for treatment of CAD and PAD

Uses/Notes

FDA has approved a new [indication](#) for rivaroxaban to reduce the risk of major cardiovascular (CV) events, such as CV death, myocardial infarction (MI) and stroke, in patients with chronic coronary or peripheral artery disease (CAD/PAD). It is now the first and only factor Xa inhibitor approved for patients with these conditions.

Approval was based on results from the [COMPASS trial](#), which showed a significant 24% reduction in the risk of major CV events in patients with chronic CAD and/or PAD with the rivaroxaban 2.5-mg vascular dose twice daily plus aspirin 100 mg once daily, compared with aspirin alone.

This finding was driven by a 42% reduction in stroke, 22% reduction in CV death, and 14% reduction in heart attack. The risk of major bleeding was significantly higher in patients taking the rivaroxaban/aspirin regimen compared with aspirin alone, with no significant increase in fatal or intracranial bleeds.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-new-indication-twice-daily-dose-treatment-cad-and-pad>

[Alerts and Recalls](#)

Generic Name (Trade Name—Company)

October 25, 2018

Methocarbamol

(Robaxin—Endo Pharmaceuticals)

Two lots of recalled product have incorrect daily dosing information on label

Uses/Notes

Endo Pharmaceuticals is voluntarily [recalling](#) two lots of methocarbamol (Robaxin) 750-mg tablets in 100-count bottle pack. The product labels contain incorrect daily dosing information, misstating the daily dose as “two to four tablets four times daily” rather than the correct dosage of “two tablets three times daily.”

Patients who follow the label directions may experience significant drowsiness or dizziness that would put them at risk of falls or an overdose that could result in seizures, coma, or death.

The product is indicated as an adjunct therapy to rest, physical therapy, and other measures to relieve the discomfort associated with acute, painful musculoskeletal conditions.

The recall includes the product lot 216702P1, expiration date September 2020; and lot 220409P1, expiration date January 2021.

To date, Endo Pharmaceuticals has not received any reports of adverse events related to this recall.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/two-lots-recalled-product-have-incorrect-daily-dosing-information-label>

[Alerts and Recalls](#)

Generic Name (Trade Name—Company)

October 25, 2018

Homeopathic aqueous-based products

(Multiple trade names—Sprayology, King Bio)

Recalled products may have microbial contamination

Uses/Notes

Sprayology is voluntarily [recalling](#) all lots within expiry from 10/18 to 7/22 of its aqueous-based homeopathic product line because of possible microbial contamination.

Administration or use of drug products with microbial contamination could result in increased infections that may require medical intervention or be life threatening to certain individuals.

The products are for assorted symptom relief and can be identified by the main label on the bottle and by the expiration date printed on the backside of the label. Each recalled product is an individual 1.38-oz. oral spray in white bottle manufactured at the King Bio facility in Asheville, NC. The product was distributed nationwide via wholesale, retail, and online sales.

View the list of recalled products [here](#).

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/recalled-products-may-have-microbial-contamination>

[Alerts and Recalls](#)

Generic Name (Trade Name—Company)

October 25, 2018

Stem cell products

(ReGen Series—Liveyon)

Possible adverse reactions prompt recall of stem cell products

Uses/Notes

In October, Liveyon, a distributor of stem cell products manufactured by Genetech and marketed under the trade name ReGen Series, voluntarily recalled the products in response to reports of possible adverse reactions.

Liveyon immediately discontinued the purchase of any product from Genetech and procured new product from an alternative manufacturer that has been in business for more than 15 years and manufactures the new product in a cGMP compliant facility. Liveyon stated that the new manufacturer is a U.S.-based, FDA-registered, fully licensed and compliant umbilical cord blood/tissue bank accredited by the America Association of Blood Banks (AABB). It is a member of the Be The Match Program and has passed all FDA inspections.

Liveyon resumed distribution of the new product line effective Monday, October 8, 2018.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/possible-adverse-reactions-prompt-recall-stem-cell-products>

[Alerts and Recalls](#)

Generic Name (Trade Name—Company)

October 25, 2018

Weight loss supplement

(Zero Xtreme—Fat Burners Zone)

Zero Xtreme weight loss product contains undeclared sibutramine

Uses/Notes

Fat Burners Zone is voluntarily [recalling](#) 1 lot of Zero Xtreme capsules in response to an FDA analysis that found the product contains sibutramine, an appetite suppressant that was withdrawn from the U.S. market because of safety concerns. The presence of sibutramine in Zero Xtreme renders it an unapproved drug for which safety and efficacy have not been established and, therefore, subject to recall.

Sibutramine is the active pharmaceutical ingredient in Meridia, a drug approved by FDA in 1997 for prescription treatment of obesity and, subsequently, withdrawn from the U.S. market on December 21, 2010, after clinical data indicated that sibutramine poses an increased risk of heart attack and stroke.

Sibutramine is known to substantially increase blood pressure and/or pulse rate in some patients and may present a significant risk for patients with a history of coronary artery disease, congestive heart failure, arrhythmias, or stroke.

This tainted product is marketed as a dietary supplement for weight loss and is packaged in gray aluminum bottles with gray aluminum caps, 30 capsules per bottle. The affected Zero Xtreme lot, #1220062085, expires 03/2020. Zero Xtreme was distributed nationwide via the internet through the website fatburnerszone.com.

To date, Fat Burners Zone has not received any reports of adverse events related to this recall.

Fat Burners Zone is notifying its distributors and customers by a recall letter sent by e-mail and is arranging for return/replacement of all recalled products.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/zero-xtreme-weight-loss-product-contains-undeclared-sibutramine>

Alerts and Recalls

Generic Name (Trade Name—Company)

October 25, 2018

Prednisolone and gatifloxacin ophthalmic solution 1%/0.5%

(No trade names—Promise Pharmacy)

Small particulate found floating in one product lot

Uses/Notes

Promise Pharmacy is voluntarily [recalling](#) one lot (09042018@2, exp. 12/03/2018) of prednisolone and gatifloxacin ophthalmic solution 1%/0.5% sterile 3-mL vials in response to report of unidentified small particulate found floating in the solution.

Potential adverse health consequences could range from limited eye irritation, inflammation, and visual impairment to permanent ocular damage with use of this eye drop solution.

The product is used as a postsurgical (cataract) ophthalmic treatment and was distributed nationwide to individual patients.

Promise Pharmacy is notifying its prescribers and patients by telephone and mail and is arranging for return, replacement, and refund of all recalled product.

Patients who have product that is being recalled should stop using it and return it to Promise Pharmacy. Patients will be sent packaging with a prepaid shipping label to facilitate prompt return of product.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/small-particulate-found-floating-one-product-lot>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

October 29, 2018

Talazoparib

(Talzenna—Pfizer)

**FDA approves talazoparib for gBRCAm
HER2-negative locally advanced or metastatic breast
cancer**

Uses/Notes

FDA approved [talazoparib](#), a poly (ADP-ribose) polymerase (PARP) inhibitor, for patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), human epidermal growth factor receptor 2–negative locally advanced or metastatic breast cancer. Patients must be selected for therapy on the basis of an FDA-approved companion diagnostic, the BRACAnalysis CDx test (Myriad Genetic Laboratories).

Approval was based on an open-label trial randomizing 431 patients (2:1) with gBRCAm HER2-negative locally advanced or metastatic breast cancer to receive talazoparib (1 mg) or physician's choice of chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine). All patients were required to have a known deleterious or suspected deleterious gBRCA mutation and must have received no more than three prior cytotoxic chemotherapy regimens for locally advanced or metastatic disease. Patients were required to have received treatment with an anthracycline and/or a taxane (unless contraindicated) in the neoadjuvant, adjuvant, and/or metastatic treatment setting.

The prescribing information includes warnings and precautions for myelodysplastic syndrome/acute myeloid leukemia, myelosuppression, and embryo–fetal toxicity. Most common (~20%) adverse reactions of any grade were fatigue, anemia, nausea, neutropenia, headache, thrombocytopenia, vomiting, alopecia, diarrhea, and decreased appetite.

The recommended talazoparib dose is 1 mg taken as a single-oral daily dose, with or without food.

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-talazoparib-gbrca-her2-negative-locally-advanced-or-metastatic>

Supplemental Approvals

Generic Name (Trade Name—Company)

October 29, 2018

Sodium oxybate

Uses/Notes

[FDA approved sodium oxybate](#) for treatment of cataplexy and excessive daytime sleepiness in pediatric patients (aged 7–17 y) with narcolepsy.

Sodium oxybate is a central nervous system (CNS) depressant approved in 2002 for treatment of cataplexy in adult patients with narcolepsy. Cataplexy is a sudden and transient episode of muscle weakness accompanied by full conscious awareness, typically triggered by emotions such as laughing, crying, or terror.

Sodium oxybate either alone or in combination with other CNS depressants may be associated with adverse reactions that include seizure, respiratory depression, decreases in the level of consciousness, coma, and death. Rapid onset of sedation, coupled with amnesia, particularly when combined with alcohol, has posed risks for voluntary and involuntary users (e.g., assault victims).

The agent is contraindicated in patients being treated with sedative hypnotic agents and in patients with succinic semialdehyde dehydrogenase deficiency. In addition, patients should not drink alcohol when using Sodium oxybate. Succinic semialdehyde deficiency is a rare inborn error of metabolism variably characterized by mental retardation, hypotonia, and ataxia.

The most common adverse reactions in pediatric patients were bed-wetting, nausea, headache, vomiting, weight decrease, decreased appetite, and dizziness.

The following adverse reactions have been identified during postapproval use of sodium oxybate. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: joint pain, decreased appetite, fall, fluid retention, hangover, headache, hypersensitivity, hypertension, memory impairment, nocturia, panic attack, vision blurred and weight decreased.

Because of the risk of serious outcomes resulting from

(Xyrem—Jazz Pharmaceuticals)

Agent now approved for treatment of cataplexy and excessive daytime sleepiness in children

inappropriate prescribing, misuse, abuse and diversion, sodium oxybate is only available through a [risk evaluation mitigation strategy \(REMS\) programs](#).

Source URL:

<http://www.aphadruonline.com/supplemental-approvals/agent-now-approved-treatment-cataplexy-and-excessive-day-time-sleepiness>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

October 30, 2018

Estradiol and progesterone capsules

(Bijuva—TherapeuticsMD)

Bioidentical hormone therapy reduces hot flashes due to menopause

Uses/Notes

FDA approved [Bijuva](#) (TherapeuticsMD), the first bioidentical oral hormone combination of estradiol and progesterone (1-mg/100-mg capsule) to treat moderate to severe hot flashes in women with a uterus.

Approval was based on the Phase III Replenish Trial, in which Bijuva demonstrated a statistically significant reduction from baseline in both the frequency and severity of hot flashes compared with placebo, while reducing the risks to the endometrium.

The most common adverse reactions (?3%) were breast tenderness, headache, vaginal bleeding, vaginal discharge, and pelvic pain. No clinically significant changes were found in lipid, coagulation, or glucose parameters compared with placebo, and no unexpected safety signals were noted.

The recommended dosage is one tablet orally each evening with food.

Bijuva comes with a boxed warning; see the [prescribing information](#) for more information.

The drug will be available in the United States in the second quarter of 2019.

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/bioidentical-hormone-therapy-reduces-hot-flashes-due-menopause>

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