
A^{PhA} **DrugInfoLine[®]**

September 2018

[OTC Medicines Corner](#)

Advising on this article: Tara Whetsel

September 4, 2018

One-dose-fits-all approach to aspirin therapy for primary prevention is not ideal

Key Point

The benefits of aspirin therapy appear to be dose dependent, with patients of higher body weight (>70 kg) requiring higher doses to prevent cardiovascular (CV) events, and similar results observed for the long-term reduction in the risk of colorectal cancer, according to results of a meta-analysis published in the Lancet.

Source URL:

<http://www.aphadruginfoline.com/otc-medicines-corner/one-dose-fits-all-approach-aspirin-therapy-primary-prevention-not-ideal>

[Focus on Lipids Care](#)

Advising on this article: Amber L. Briggs

September 4, 2018

Lipid-lowering benefits on clinical outcomes relative to baseline LDL value

Key Point

A meta-analysis published in JAMA of 34 trials involving more than 270,000 patients showed that more intensive LDL-lowering therapy compared with less-intensive therapy resulted in a greater reduction in the risk of all-cause and cardiovascular (CV) mortality, but only in patients with baseline LDL levels of 100 mg/dL or more.

Source URL:

<http://www.aphadruginfoline.com/focus-lipids-care/lipid-lowering-benefits-clinical-outcomes-relative-baseline-ldl-value>

[Nephrology](#)

Advising on this article: Edward F. Foote, Sarah Ray

September 11, 2018

Apixaban is an option for anticoagulation in patients on dialysis

Key Point

Use of standard-dose apixaban (Eliquis—Bristol-Myers Squibb, Pfizer) in patients with atrial fibrillation (AF) and end-stage renal disease (ESRD) who are on dialysis was associated with a significantly lower risk of stroke/embolism, death, and major bleeding compared with warfarin, according to results of an observational study published in *Circulation*.

Source URL:

<http://www.aphadruginfoline.com/nephrology/apixaban-option-anticoagulation-patients-dialysis>

[Focus on Diabetes Care](#)

Advising on this article: Charles D. Ponte

September 11, 2018

Sulfonylureas as second-line agents increase the risk of adverse outcomes

Key Point

Adding sulfonylurea to metformin therapy or switching metformin to a sulfonylurea in patients with type 2 diabetes resulted in an increased risk of myocardial infarction (MI), all-cause mortality, and severe hypoglycemia compared with metformin monotherapy, according to results of an observational study published in BMJ.

Source URL:

<http://www.aphadruginfoline.com/focus-diabetes-care/sulfonylureas-second-line-agents-increase-risk-adverse-outcomes>

[Alternative Medicines Corner](#)

Advising on this article: Nicole M. Maisch

September 18, 2018

Complementary medicines associated with poor outcomes in patients with cancer

Key Point

Patients with cancer who used complementary medicines had higher refusal rates of surgery, chemotherapy, radiotherapy, and hormone therapy compared with those who did not use these alternative therapies, resulting in greater risk of death, according to results of a retrospective observational study published in JAMA Oncology.

Source URL:

<http://www.aphadruginfoline.com/alternative-medicines-corner/complementary-medicines-associated-poor-outcomes-patients-cancer>

[Endocrinology](#)

Advising on this article:

September 18, 2018

Vitamin D levels associated with better pregnancy outcomes

Key Point

In women with a history of pregnancy losses and no diagnosis of infertility, those with sufficient preconception vitamin D serum levels had increased pregnancy rates and live births compared with women who had insufficient levels, according to a report published in The Lancet Diabetes and Endocrinology.

Source URL:

<http://www.aphadruonline.com/endocrinology/vitamin-d-levels-associated-better-pregnancy-outcomes>

[Psychiatry](#)

Advising on this article: M. Lynn Crismon

September 25, 2018

Unsafe use of zolpidem is common

Key Point

An assessment of national survey data from 2015 showed that many patients used zolpidem in unsafe ways, such as by administering higher-than-recommended doses (females and older adults), using the drug for a sustained period, and combining it with other central nervous system (CNS) depressants.

Source URL:

<http://www.aphadruginfo.com/psychiatry/unsafe-use-zolpidem-common>

[Focus on Lipids Care](#)

Advising on this article: Amber L. Briggs

September 25, 2018

Statins decrease osteoporosis and fracture risk after stroke

Key Point

Patients who used statins after a stroke had a reduced risk of osteoporosis, hip fracture, and vertebral fracture compared with those who did not use statins, with a dose-effect relationship observed, according to results of an observational study published in the Journal of Clinical Endocrinology and Metabolism.

Source URL:

<http://www.aphadruginfo.com/focus-lipids-care/statins-decrease-osteoporosis-and-fracture-risk-after-stroke>

Alerts and Recalls

Generic Name (Trade Name—Company)

September 4, 2018

Montelukast

(No trade name—Camber Pharmaceuticals)

Bottles labeled as montelukast contain different drug

Uses/Notes

[FDA is warning](#) consumers and health professionals about a voluntary recall of one lot of montelukast sodium tablets (lot #MON17384, expiration 12/31/2019) by Camber Pharmaceuticals. Sealed bottles labeled as montelukast sodium tablets, 10 mg, 30-count bottle were found to instead contain 90 tablets of losartan potassium tablets, 50 mg.

This tablet mix-up may pose a safety risk because taking losartan tablets when not prescribed has the potential to cause renal dysfunction, elevated potassium levels, and low blood pressure. This risk is especially high for pregnant women taking the allergy and asthma medication montelukast because losartan, which is indicated to treat high blood pressure, could harm or kill the fetus.

FDA recommends that consumers who have this recalled product contact their health care provider or pharmacist immediately.

Montelukast sodium tablets are beige, rounded square-shaped, film coated tablets that are imprinted with “I” on one side and “114” on the reverse. Losartan tablets are white and oval-shaped with the letter “I” imprinted on one side and the number “5” imprinted on the reverse.

This recall is not related to the recent valsartan recalls that were due to an impurity, *N*-nitrosodimethylamine (NDMA).

To date, Camber has not received adverse event reports associated with this recall.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/bottles-labeled-montelukast-contain-different-drug>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

September 4, 2018

Doravirine, lamivudine, tenofovir disoproxil fumarate; doravirine

Uses/Notes

[Merck announced](#) FDA approval of two new HIV-1 medications for adult patients with no prior antiretroviral treatment experience: a once-daily fixed-dose combination tablet of doravirine 100 mg, lamivudine (3TC) 300 mg, and tenofovir disoproxil fumarate (TDF) 300 mg, approved under the trade name Delstrigo; and doravirine 100 mg, a new nonnucleoside reverse transcriptase inhibitor that is administered in combination with other antiretroviral medicines and was approved under the trade name Pifeltro.

Both drugs are administered orally once daily with or without food.

Approval was based on findings from two pivotal, randomized, multicenter, double-blind, active controlled Phase III trials, DRIVE-AHEAD and DRIVE-FORWARD.

Delstrigo is contraindicated in patients with a previous hypersensitivity reaction to 3TC.

Delstrigo and Pifeltro are contraindicated when coadministered with drugs that are strong CYP450 3A enzyme inducers because significant decreases in doravirine plasma concentrations may occur and lessen their effectiveness.

Immune reconstitution syndrome can occur, including autoimmune disorders with variable time to onset, which may necessitate further evaluation and treatment.

Renal impairment, including acute renal failure and Fanconi syndrome, has been reported with use of TDF. Delstrigo should be avoided with concurrent or recent use of a nephrotoxic agent, as cases of acute renal failure after initiation of high-dose or multiple NSAIDs have been reported in patients with risk factors for renal dysfunction who appeared stable on TDF.

Common adverse reactions in clinical trials included dizziness (7%), nausea (5%) and abnormal dreams (5%).

Delstrigo and Pifeltro do not cure HIV-1 infection or

(Delstrigo; Pifeltro—Merck)

AIDS.

FDA approves two new HIV-1 medications

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-two-new-hiv-1-medications>

Alerts and Recalls

Generic Name (Trade Name—Company)

September 11, 2018

Dolutegravir-containing medications

(Tivicay, Juluca, Triumeq—ViiV Healthcare)

FDA warns of potential risk of neural tube birth defects with dolutegravir

Uses/Notes

[FDA is alerting](#) the public that serious cases of neural tube birth defects involving the brain, spine, and spinal cord have been reported in babies born to women treated with dolutegravir, an antiretroviral medication used to treat HIV. Approved in 2013, dolutegravir has been on the market for 5 years and is available as a single-ingredient product under the brand name Tivicay and as a fixed-dose combination tablet with other HIV medications under the brand names Juluca and Triumeq.

Preliminary results from an ongoing observational study in Botswana found that women who received dolutegravir at the time of becoming pregnant or early in the first trimester appeared to be at higher risk for these defects.

Health professionals should inform women of childbearing age about the potential risk of neural tube defects when a dolutegravir-containing regimen is used at the time of conception and early in pregnancy.

Patients should not stop taking dolutegravir without first talking to their health professional because stopping the medicine can cause the HIV infection to worsen. Stopping dolutegravir without first talking to a prescriber can cause the HIV infection to become worse.

More information is available on FDA's [website](#).

To date, in this observational study there are no reported cases of babies born with neural tube defects to women starting dolutegravir later in pregnancy. FDA said it is investigating this new safety issue and will update the public when it has more information. Ongoing monitoring will continue as part of the observational study in Botswana.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/fda-warns-potential-risk-neural-tube-birth-defects-dolutegravir>

[Alerts and Recalls](#)

Generic Name (Trade Name—Company)

September 11, 2018

Multiple generic names

(Multiple trade names—Beaumont Bio Med Inc.)

FDA alerts consumers to voluntary recall of Beaumont Bio Med's homeopathic products

Uses/Notes

FDA is alerting consumers and health professionals to a voluntary [recall](#) of all water- and alcohol-based Beaumont Bio Med Inc. (Grand Rapids, MI) drug products. These products, labeled as homeopathic, are being recalled due to microbial contamination at the manufacturing facility.

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.

These products were manufactured at the [King Bio, Inc.](#), facility in Asheville, NC. Previously, [FDA alerted consumers to HelloLife's voluntary recall of drug products labeled as homeopathic](#), also manufactured by King Bio.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/fda-alerts-consumers-voluntary-recall-beaumont-bio-meds-homeopathic-products>

[Supplemental Approvals](#)

Generic Name (Trade Name—Company)

September 11, 2018

Buprenorphine and naloxone

(Cassipa—Teva)

FDA approves new sublingual formulation for maintenance treatment of opioid dependence

Uses/Notes

FDA has [approved](#) buprenorphine and naloxone sublingual film under the trade name Cassipa for maintenance treatment of opioid dependence. This action provides a new dosage strength (16 mg/4 mg) of the sublingual film, which is also approved in both brand name and generic versions and in various strengths.

Cassipa should be used as part of a complete treatment plan that includes counseling and psychosocial support and should be used only after patient induction and stabilization up to a dose of 16 mg of buprenorphine using another marketed product.

Common adverse events are oral numbness, burning mouth, inflammation of oral mucous membrane, headache, nausea, vomiting, excessive sweating, constipation, signs and symptoms of withdrawal, insomnia, pain, and peripheral edema.

These products may only be prescribed by Drug Addiction Treatment Act–certified prescribers.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-new-sublingual-formulation-maintenance-treatment-opioid>

[Supplemental Approvals](#)

Generic Name (Trade Name—Company)

September 11, 2018

Riluzole oral suspension

(Tiglutik—ITF Pharma)

First easy-to-swallow riluzole liquid approved for treatment of ALS

Uses/Notes

FDA has [approved](#) riluzole oral suspension for the treatment of amyotrophic lateral sclerosis (ALS). It is the first and only easy-to-swallow thickened riluzole liquid for ALS and is administered twice daily via an oral syringe.

Approval was based on bioavailability studies comparing oral riluzole tablets to riluzole oral suspension. While riluzole's mechanism of action is not fully understood, in clinical studies it has been shown repeatedly to modulate glutamate neurotransmission by inhibiting both glutamate release and postsynaptic glutamate receptor signaling.

The most common adverse effects of the oral suspension are consistent with the established clinical profile of riluzole and include oral hypoesthesia, asthenia, nausea, decreased lung function, hypertension, and abdominal pain.

Riluzole oral suspension has received orphan drug designation from FDA. The product will be available in mid-October.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/first-easy-swallow-riluzole-liquid-approved-treatment-als>

[Alerts and Recalls](#)

Generic Name (Trade Name—Company)

September 11, 2018

Multiple generic names

(Multiple trade names—Pharm D Solutions)

Pharm D Solutions recalls all sterile compounded drug products

Uses/Notes

Pharm D Solutions is voluntarily [recalling](#) all sterile compounded drug products dispensed with the past 12 months because of concerns that practices at the pharmacy may pose a risk of contamination to products intended to be sterile. These concerns arose following a routine inspection of the pharmacy by FDA.

Administration of a nonsterile product that is intended to be sterile by S.C., I.M., I.V., or ocular routes of administration may result in serious injury or death.

Pharm D Solutions stated that to date, it is not aware of any adverse events related to this recall nor any indication that the compounded sterile drug products being recalled are actually contaminated. No medications or any component thereof have been shown to be nonsterile.

The recall encompasses all compounded sterile drug products, within expiry, that were dispensed within the last twelve months. The sterile drug products subject to this recall were distributed nationwide and directly to customers and/or medical facilities. The recall does not affect the pharmacy's nonsterile compounded products or retail pharmacy operations.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/pharm-d-solutions-recalls-all-sterile-compounded-drug-products>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

September 26, 2018

Moxetumomab pasudotox-tdfk

Uses/Notes

FDA [approved](#) moxetumomab pasudotox-tdfk injection for I.V. use for the treatment of adult patients with relapsed or refractory hairy cell leukemia (HCL) who have received at least two prior systemic therapies, including treatment with a purine nucleoside analog. The agent is a CD22-directed cytotoxin and is the first of this type of treatment for patients with HCL.

HCL is a rare, slow-growing cancer of the blood in which the bone marrow makes too many lymphocytes. HCL is named after these extra B cells, which look “hairy” when viewed under a microscope. As the number of leukemia cells increases, fewer healthy white blood cells, red blood cells, and platelets are produced.

Efficacy of the agent was studied in a single-arm, open-label clinical trial of 80 patients who had received prior treatment for HCL with at least two systemic therapies, including a purine nucleoside analog. The trial measured durable complete response (CR), defined as maintenance of hematologic remission for more than 180 days after achievement of CR. Thirty percent of patients in the trial achieved durable CR, and the overall response rate (number of patients with partial or complete response to therapy) was 75%.

Common adverse effects include infusion-related reactions, edema, nausea, fatigue, headache, fever, constipation, anemia, and diarrhea.

The prescribing information includes a boxed warning to advise health professionals and patients about the risk of developing capillary leak syndrome, a condition in which fluid and proteins leak out of tiny blood vessels into surrounding tissues. Symptoms of capillary leak syndrome include difficulty breathing, weight gain, hypotension, or swelling of arms, legs, and/or face.

The boxed warning also notes the risk of hemolytic uremic syndrome, a condition caused by the abnormal destruction of red blood cells. Patients should be made aware of the importance of maintaining adequate fluid intake, and blood chemistry values should be monitored frequently.

(Lumoxiti—AstraZeneca)

FDA approves new kind of treatment for hairy cell leukemia

Other serious warnings include decreased renal function, infusion-related reactions, and electrolyte abnormalities. Women who are breastfeeding should not take the drug.

Source URL:

<http://www.aphadruonline.com/new-drug-approvals/fda-approves-new-kind-treatment-hairy-cell-leukemia>

Supplemental Approvals

Generic Name (Trade Name—Company)

September 26, 2018

Latanoprost ophthalmic emulsion 0.005%

(Xelpros—Sun Pharma)

Topical formulation reduces IOP in open-angle glaucoma or ocular hypertension

Uses/Notes

Sun Pharma [announced](#) FDA approval of latanoprost ophthalmic emulsion 0.005% for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

It is the first and only form of latanoprost that is not formulated with benzalkonium chloride, a preservative commonly used in topical ocular preparations.

Recommended dosage is one drop in the affected eye(s) once daily in the evening. If one dose is missed, treatment should continue with the next dose as normal. Reduction of IOP starts approximately 3 to 4 hours after administration, and the maximum effect is reached after 8 to 12 hours.

In clinical trials, the most frequently reported adverse reactions were eye pain/stinging upon instillation and ocular hyperemia (redness).

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/topical-formulation-reduces-iop-open-angle-glaucoma-or-ocular-hypertension>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

September 26, 2018

Duvelisib

Uses/Notes

FDA granted regular [approval](#) to duvelisib for adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies.

In addition, duvelisib received accelerated approval for adult patients with relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies.

The CLL and SLL indication is based on a randomized, multicenter, open-label trial comparing duvelisib with ofatumumab in patients with relapsed or refractory CLL or SLL. The trial randomized patients (1:1) to either duvelisib 25 mg orally twice daily or ofatumumab.

Ofatumumab was administered intravenously at an initial dose of 300 mg, followed 1 week later by 2,000 mg once weekly for seven doses, then 2,000 mg once every 4 weeks for four additional doses.

Among 196 patients receiving at least two prior therapies (95 randomized to duvelisib, 101 to ofatumumab), the estimated median progression-free survival, as assessed by an independent review committee, was 16.4 months in the duvelisib arm and 9.1 months in the ofatumumab arm (hazard ratio of 0.40; standard error 0.2). The overall response rate (ORR) was 78% and 39% for the duvelisib and ofatumumab arms, respectively (39% difference, standard error 6.5%).

The FL indication is based on a single-arm multicenter trial of duvelisib enrolling 83 patients with FL who were refractory to rituximab and to either chemotherapy or radioimmunotherapy. The ORR was 42% (95% CI 31–54), with 41% of patients experiencing partial responses and one patient having a complete response.

Of the 35 responding patients, 15 (43%) maintained responses for at least 6 months, and 6 (17%) maintained responses for at least 12 months. Continued approval for the FL indication may be contingent on verification of clinical benefit demonstrated in a planned randomized

(Copiktra—Verastem)

New drug targets relapsed or refractory forms of leukemia and lymphoma in adults

trial.

The prescribing information contains boxed warnings for fatal and/or serious infections, diarrhea or colitis, cutaneous reactions, and pneumonitis, and warnings for neutropenia and hepatotoxicity.

Of 442 patients with hematologic malignancies treated with duvelisib at the approved dose, 65% had serious adverse reactions, with the most frequent being infection, diarrhea or colitis, and pneumonia.

The most common adverse reactions (?20%) were diarrhea or colitis, neutropenia, rash, fatigue, pyrexia, cough, nausea, upper respiratory infection, pneumonia, musculoskeletal pain, and anemia. Adverse reactions resulted in permanent discontinuation of duvelisib in 35% of patients. Dose reduction occurred in 24%.

The recommended duvelisib dose is 25 mg orally twice daily, taken continuously in 28-day treatment cycles.

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/new-drug-targets-relapsed-or-refractory-forms-leukemia-and-lymphoma-adults>

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