
A^{PhA} **DrugInfoLine[®]**

November 2018

[Cardiology](#)

Advising on this article: Eric MacLaughlin

November 5, 2018

A bleak picture of aspirin for primary prevention in older adults

Key Point

Three publications in the New England Journal of Medicine from the ASPREE trial showed that daily use of low-dose aspirin in healthy, community-dwelling older people without documented cardiovascular (CV) disease, dementia, or physical disability did not prolong disability-free survival, did not reduce the risk of CV disease (CVD), and was associated with a higher risk of all-cause mortality and major hemorrhage compared with placebo.

Source URL:

<http://www.aphadruginfoline.com/cardiology/bleak-picture-aspirin-primary-prevention-older-adults>

[Respiratory](#)

Advising on this article: Roy A. Pleasants, II

November 5, 2018

A personalized approach to COPD management is needed

Key Point

A small decline in lung function with no change in the rate of exacerbations was observed in patients with infrequent exacerbations and moderate to severe chronic obstructive pulmonary disease (COPD) who had been on long-term triple therapy and were subsequently de-escalated to dual therapy, according to data published in the American Journal of Respiratory and Critical Care Medicine.

Source URL:

<http://www.aphadruginfoline.com/respiratory/personalized-approach-copd-management-needed>

[OTC Medicines Corner](#)

Advising on this article: Tara Whetsel

November 13, 2018

Folic acid and multivitamin use may decrease autism risk

Key Point

Maternal exposure to folic acid and/or multivitamins (MVI) before and during pregnancy was associated with a lower risk of autism spectrum disorder in the child compared with no exposure, according to results of a case-control study published in JAMA Psychiatry.

Source URL:

<http://www.aphadruonline.com/otc-medicines-corner/folic-acid-and-multivitamin-use-may-decrease-autism-risk>

[Focus on Immunizations](#)

Advising on this article: John D. Grabenstein

November 13, 2018

Adolescent vaccinations not associated with fertility problems

Key Point

Adolescent vaccinations with HPV, Tdap, inactivated influenza, and meningococcal conjugate (MenACWY) were not associated with an increased risk of primary ovarian insufficiency, according to results of a retrospective cohort study published in Pediatrics.

Source URL:

<http://www.aphadruginfoline.com/focus-immunizations/adolescent-vaccinations-not-associated-fertility-problems>

Supplemental Approvals

Generic Name (Trade Name—Company)

November 1, 2018

Pembrolizumab

(Keytruda—Merck)

In combination with chemotherapy, drug approved for first-line treatment of metastatic squamous NSCLC

Uses/Notes

[FDA approved](#) a new indication for pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment of metastatic squamous non-small cell lung cancer (NSCLC).

Approval was based on a randomized, multicenter, double-blind, placebo-controlled trial in 559 patients with metastatic squamous NSCLC, regardless of PD-L1 tumor expression status, who had not previously received systemic therapy for metastatic disease.

Patients were randomized (1:1) to pembrolizumab 200 mg or placebo in combination with carboplatin, along with either paclitaxel every 3 weeks or nab-paclitaxel weekly on a 3-week cycle for four cycles, followed by pembrolizumab or placebo. Patients continued pembrolizumab or placebo until disease progression, unacceptable toxicity, or a maximum of 24 months.

The trial demonstrated statistically significant improvements in patients receiving pembrolizumab plus chemotherapy compared with those randomized to placebo plus chemotherapy.

The most common adverse reactions in at least 20% of patients who received pembrolizumab were fatigue/asthenia, nausea, constipation, diarrhea, vomiting, pyrexia, decreased appetite, rash, cough, dyspnea, alopecia, and peripheral neuropathy.

The recommended pembrolizumab dose for metastatic squamous NSCLC is 200 mg intravenously every 3 weeks, prior to chemotherapy when given on the same day, until disease progression, unacceptable toxicity, or 24 months after initiation.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/combination-chemotherapy-drug-approved-first-line-treatment-metastatic>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

November 1, 2018

Adalimumab-adaz

(Hyrimoz—Sandoz)

Sandoz receives FDA approval for adalimumab biosimilar

Uses/Notes

[Sandoz announced](#) FDA approval of adalimumab-adaz (Hyrimoz), a biosimilar to adalimumab (Humira), for treatment of rheumatoid arthritis, juvenile idiopathic arthritis in patients aged 4 years and older, psoriatic arthritis, ankylosing spondylitis, adult Crohn's disease, ulcerative colitis, and plaque psoriasis.

The drug, a tumor necrosis factor inhibitor administered subcutaneously by injection, is the third FDA-approved biosimilar to adalimumab.

Approval was based on a randomized, double-blind, three-arm, parallel biosimilarity study that confirmed the pharmacokinetics, immunogenicity, and safety of adalimumab-adaz. The study met the primary endpoint, demonstrating bioequivalence for all primary pharmacokinetic parameters.

A confirmatory efficacy and safety biosimilarity study demonstrated therapeutic equivalence in the sensitive indication of patients with moderate to severe chronic plaque-type psoriasis, with a similar safety and immunogenicity profile to the reference biologic.

The most common adverse reactions (incidence > 10%) were infections (e.g., upper respiratory, sinusitis), injection-site reactions, headache, and rash.

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/sandoz-receives-fda-approval-adalimumab-biosimilar>

Alerts and Recalls

Generic Name (Trade Name—Company)

November 1, 2018

Irbesartan

Uses/Notes

[FDA is alerting](#) patients and health professionals to ScieGen's voluntary [recall](#) of certain lots of irbesartan, an angiotensin II receptor blocker (ARB), because they contain *N*-nitrosodiethylamine (NDEA), a known animal and suspected human carcinogen.

FDA laboratory testing confirmed NDEA in some lots of ScieGen's irbesartan. ScieGen's irbesartan products are labeled as Westminster Pharmaceuticals and Golden State Medical Supply (GSMS). See the [list of irbesartan products under recall](#).

This is the first nonvalsartan drug product the agency has found to contain the NDEA impurity.

In addition, Aurobindo, which manufactures the active pharmaceutical ingredient (API) for ScieGen's irbesartan products, is [recalling](#) all unexpired lots of its irbesartan API supplied to the U.S. market with NDEA. FDA and Aurobindo laboratory testing confirmed NDEA in certain lots of the Aurobindo's irbesartan API.

FDA reminds patients taking any recalled ARB to continue taking their current medicine until their pharmacist provides a replacement or their doctor provides an alternative treatment option. Not all ARBs contain NDEA or *N*-nitrosodimethylamine (NDMA), so pharmacists may be able to provide a refill of medication not affected by the recall, or doctors may prescribe a different medication that treats the same condition.

To date, ScieGen is the only manufacturer of irbesartan drug products found to contain NDEA.

FDA continues to test all ARBs for the presence of impurities and has publicly posted two methods for manufacturers and regulatory agencies around the world to test their ARBs for the unexpected NDMA and NDEA impurities. The [combined headspace method](#) and the [combined direct injection method](#) can detect and quantify NDMA and NDEA simultaneously in ARB API and finished drug products.

FDA continues to work with API and drug manufacturers

(No trade names—*ScieGen*)

Some lots of irbesartan recalled because they contain NDEA carcinogen

to ensure their products are not at risk for NDMA or NDEA formation.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/some-lots-irbesartan-recalled-because-they-contain-ndea-carcinogen>

[Alerts and Recalls](#)

Generic Name (Trade Name—Company)

November 1, 2018

Irbesartan

(No trade names—Aurobindo)

Aurobindo recalls 22 batches of drug substance because of NDEA impurity

Uses/Notes

[Aurobindo Pharma is voluntarily recalling](#) 22 batches of irbesartan drug substance because they contain *N*-nitrosodiethylamine (NDEA). NDEA, which occurs naturally in certain foods, drinking water, air pollution, and industrial processes, has been classified as a probable human carcinogen by the International Agency for Research on Cancer.

These 22 batches of irbesartan drug substance were supplied to ScieGen Pharmaceuticals to manufacture the finished irbesartan drug product.

Aurobindo has notified ScieGen of the recall and is arranging for the return of all available irbesartan drug substance. Aurobindo Pharma Limited has further advised ScieGen to contact its distributors and retailers to return irbesartan drug product and finished irbesartan tablets that have been identified by Aurobindo.

Patients should contact their pharmacist or physician for advise on an alternative treatment before returning their medication. Patients who are on irbesartan should continue taking their medication, as the risk of harm to a patient's health may be higher if treatment is stopped immediately without an alternative treatment.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/aurobindo-recalls-22-batches-drug-substance-because-ndea-impurity>

[Alerts and Recalls](#)

Generic Name (Trade Name—Company)

November 13, 2018

Epinephrine auto-injectors

(EpiPen, Epi-Pen Jr.—Mylan)

Some EpiPen auto-injectors may not readily slide out of carrier tube

Uses/Notes

FDA is alerting patients, caregivers, and health professionals that the labels attached to some EpiPen 0.3 mg and EpiPen Jr 0.15 mg auto-injectors, and the authorized generic versions, may block access to the auto-injector and prevent the ability to easily access the product.

In a [letter](#) to health professionals from Pfizer, the manufacturer of the Mylan EpiPen, the label sticker on the auto-injector unit may have been improperly applied, causing resistance when removing it from the carrier tube. The carrier tube is the immediate package in which the auto-injector is contained. In some cases, the patient or caregiver may not be able to quickly remove the epinephrine auto-injector from the carrier tube.

The auto-injector device and the epinephrine it delivers are not affected by this issue and can be used as prescribed. It is vital for lifesaving products to work as designed in an emergency situation, and patients and caregivers should inspect their epinephrine auto-injector prior to needing it to ensure they can quickly access the product.

The letter also describes how to inspect potentially affected products and explains that patients should contact Mylan Customer Relations at 800-796-9526 if an auto-injector does not slide out easily from the carrier tube OR the label is not fully adhered to the auto-injector. Pharmacists should inspect the products before dispensing them to patients to ensure quick access to the auto-injector and should not dispense any product that does not slide easily out of its carrier tube.

FDA is not aware of any adverse event reports associated with improperly applied EpiPen or EpiPen Jr auto-injectors, or their authorized generics label. As stated on the product label, consumers should always seek emergency medical help right away after using their epinephrine auto-injector.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/some-epipen-auto-injectors-may-not-readily-slide-out-carrier-tube>

Supplemental Approvals

Generic Name (Trade Name—Company)

November 13, 2018

Lorlatinib

(Lorbrena—Pfizer)

**Lorlatinib approved for previously treated
ALK-positive metastatic NSCLC**

Uses/Notes

[Pfizer announced](#) FDA approval of a new indication for lorlatinib, a third-generation anaplastic lymphoma kinase (ALK) tyrosine kinase inhibitor (TKI) for patients with ALK-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on crizotinib and at least one other ALK inhibitor for metastatic disease; or whose disease has progressed on alectinib or ceritinib as the first ALK inhibitor therapy for metastatic disease.

Accelerated approval was based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

While many ALK-positive metastatic NSCLC patients respond to initial TKI therapy, they typically experience tumor progression, stated Pfizer in a news release. In addition, options for patients who progress after treatment with second-generation ALK TKIs, alectinib, brigatinib and ceritinib, are limited. Approval of this indication represents a new option for patients who have progressed on a second-generation ALK TKI, providing an opportunity to remain on oral therapy.

In clinical trials, the most common (~20%) adverse reactions were edema, peripheral neuropathy, cognitive effects, dyspnea, fatigue, weight gain, arthralgia, mood effects, and diarrhea.
increased alkaline phosphatase.

The most frequent serious adverse reactions reported were pneumonia, dyspnea, pyrexia, mental status changes, and respiratory failure.

Fatal adverse reactions occurred in 2.7% percent of patients and included pneumonia, myocardial infarction, acute pulmonary edema, embolism, peripheral artery occlusion, and respiratory distress.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/lorlatinib-approved-previously-treated-alk-positive-metastatic-nsclc>

[New Drug Approvals](#)

Generic Name (Trade Name—Company)

November 13, 2018

Revefenacin inhalation solution

(Yupelri—Theravance BioPharma, Mylan)

New drug approved for maintenance treatment of adults with COPD

Uses/Notes

FDA approved [revefenacin inhalation solution](#) for maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Revefenacin is a long-acting muscarinic antagonist, a class of medicines that improve lung function in patients with COPD. Revefenacin is an inhalation solution that is administered once daily via a standard jet nebulizer.

As with other inhaled medicines, revefenacin can cause paradoxical bronchospasm (wheezing). If paradoxical bronchospasm occurs, patients should discontinue use. Patients should also be alert for signs and symptoms of acute narrow-angle glaucoma (e.g., eye pain or discomfort, blurred vision, visual changes). Patients should consult a health professional immediately if any of these signs or symptoms develop.

The most common adverse reactions include cough, nasopharyngitis, upper respiratory tract infection, headache, and back pain. Health professionals should avoid administering revefenacin with other anticholinergic-containing drugs. The agency does not recommend administering revefenacin at the same time as OATP1B1 and OATP1B3 inhibitors (e.g. rifampicin, cyclosporine, etc.), as it may lead to an increase in exposure of the active metabolite.

Source URL:

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

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