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# **A<sup>PhA</sup>** **DrugInfoLine<sup>®</sup>**

**July 2018**

## [Cardiology](#)

Advising on this article: Eric MacLaughlin

**July 2, 2018**

# **Self-monitoring results in better BP control than clinic-based monitoring**

## **Key Point**

Results of a large, 12-month, open-label, multicenter trial in patients with uncontrolled hypertension showed that self-monitoring (SM) of blood pressure (BP) with or without telemonitoring (TM) resulted in better BP control compared with clinic-based BP monitoring. Primary care clinicians were better able to titrate antihypertensive medications to meet recommended goals.

## **Source URL:**

<http://www.aphadruginfoline.com/cardiology/self-monitoring-results-better-bp-control-clinic-based-monitoring>

## [Gastroenterology](#)

Advising on this article: C. Wayne Weart

**July 2, 2018**

# **Corticosteroids for severe alcoholic hepatitis improve short-term outcomes**

## **Key Point**

According to a study published in *Gastroenterology*, use of corticosteroids in patients with severe alcoholic hepatitis significantly reduced the risk of death within 28 days when compared with controls or pentoxifylline. However, no difference was seen in 6-month mortality for any treatment or controls.

## **Source URL:**

<http://www.aphadruginfoline.com/gastroenterology/corticosteroids-severe-alcoholic-hepatitis-improve-short-term-outcomes>

## [Focus on Immunizations](#)

Advising on this article: John D. Grabenstein

**July 9, 2018**

# **Communication strategies to improve HPV vaccination rates**

## **Key Point**

Providers with a persistent communication style that focuses on the benefits of HPV vaccine and a strong recommendation to accept vaccination resulted in much higher same-day vaccination rates compared with acquiescence and agreement to defer the vaccination, according to a study published in *Pediatrics*.

## **Source URL:**

<http://www.aphadruginfoline.com/focus-immunizations/communication-strategies-improve-hpv-vaccination-rates>

## [Cardiology](#)

Advising on this article: Eric MacLaughlin

**July 9, 2018**

# **Vitamins and mineral supplements have little benefit on CV outcomes**

## **Key Point**

No significant benefits were observed with use of multivitamins, vitamin D, calcium, or vitamin C on cardiovascular (CV) outcomes or all-cause mortality. Only low- to moderate-quality evidence supports use of folic acid to reduce CV disease and folic acid and B vitamins to reduce the risk of stroke, according to results of systematic reviews and meta-analyses published in the Journal of the American College of Cardiology.

## **Source URL:**

<http://www.aphadruginfoline.com/cardiology/vitamins-and-mineral-supplements-have-little-benefit-cv-outcomes>

## [Drug Interactions Corner](#)

Advising on this article: Daniel S. Streetman

**July 16, 2018**

# **Drug interactions are common among older adults receiving antiretroviral therapies**

## **Key Point**

A cross-sectional observational study published in the Journal of Acquired Immune Deficiency Syndromes involving 744 patients with HIV receiving antiretroviral treatment and at least one nonantiretroviral medication showed that more than one-half of these patients had at least one or more potential drug–drug interactions (DDIs), with a higher risk of interactions observed for those receiving five or more medications.

## **Source URL:**

<http://www.aphadruginfoline.com/drug-interactions-corner/drug-interactions-are-common-among-older-adults-receiving-antiretroviral>

## [Pharmacogenomics Corner](#)

Advising on this article: Mary W. Roederer

**July 16, 2018**

# **Pharmacogenetic-based decision tools are not interchangeable**

## **Key Point**

A comparison of four commercially available pharmacogenetic-based decision tools in patients with major depressive disorder (MDD) and numerous treatment failures showed that genotype and predicted phenotype agreement varied substantially, as did medication recommendations, indicating these tests cannot be considered equivalent or interchangeable.

## **Source URL:**

<http://www.aphadruginfoline.com/pharmacogenomics-corner/pharmacogenetic-based-decision-tools-are-not-interchangeable>

## [Respiratory](#)

Advising on this article: Roy A. Pleasants, II

**July 24, 2018**

# **Nicotine preloading may be beneficial for smoking cessation**

## **Key Point**

Use of a nicotine patch worn for 4 weeks before attempting to quit smoking resulted in higher odds of abstinence at 4 weeks, 6 months, and 12 months compared with no nicotine preloading, but only after adjustments were made for subsequent varenicline use in the two groups.

## **Source URL:**

<http://www.aphadruonline.com/respiratory/nicotine-preloading-may-be-beneficial-smoking-cessation>

## [Focus on Diabetes Care](#)

Advising on this article: Charles D. Ponte

**July 24, 2018**

# **Metformin and the risk of acidosis in patients with kidney disease**

## **Key Point**

Use of metformin in patients with an estimated glomerular filtration rate (eGFR) between 30 mL/min/1.73 m<sup>2</sup> and 45 mL/min/1.73 m<sup>2</sup> did not result in an increased risk of incident acidosis compared with alternative diabetes treatments, according to data from two large retrospective cohort analyses.

## **Source URL:**

<http://www.aphadruginfoline.com/focus-diabetes-care/metformin-and-risk-acidosis-patients-kidney-disease>

## [Psychiatry](#)

Advising on this article: M. Lynn Crismon

**July 30, 2018**

# **Depression may result from adverse medication effects**

## **Key Point**

A U.S. population-based survey conducted over a 10-year period showed that a little more than one-third of patients used medications that list depression as a potential adverse effect, and the occurrence of depression was higher among patients who used multiple agents. compared with those not using such medications, according to a report in JAMA.

## **Source URL:**

<http://www.aphadruginfoline.com/psychiatry/depression-may-result-adverse-medication-effects>

## [Neurology](#)

Advising on this article: Jack J. Chen

**July 30, 2018**

# **Fingolimod and dimethyl fumarate appear to have similar efficacy for MS**

## **Key Point**

Use of fingolimod (Gilenya—Novartis) or delayed-release dimethyl fumarate (Tecfidera—Biogen) for patients with relapsing-remitting multiple sclerosis (RRMS) appears to have similar efficacy for treatment-naive patients, but use of fingolimod appears to have superior efficacy in treatment-experienced patients, according to results of an observational study published in *Neurology*.

## **Source URL:**

<http://www.aphadruginfoline.com/neurology/fingolimod-and-dimethyl-fumarate-appear-have-similar-efficacy-ms>

## [Alerts and Recalls](#)

### Generic Name (Trade Name—Company)

July 9, 2018

### Celecoxib

### Uses/Notes

FDA approved a [labeling supplement](#) for celecoxib, a COX-2 selective NSAID, to include results from a postmarketing cardiovascular outcomes trial that found that at the lowest dose, cardiovascular safety of celecoxib was similar to that of moderate doses of naproxen and ibuprofen.

Concerns about the cardiovascular thrombotic risk of COX-2 selective NSAIDs emerged in the early 2000s. Following an FDA Advisory Committee meeting held in 2005, which considered data from large clinical outcome trials in a wide range of indications and epidemiology studies of several individual NSAIDs, FDA concluded that the risk for cardiovascular thrombotic events was present for both COX-2 selective NSAIDs and nonselective NSAIDs.

The Prospective Randomized Evaluation of Celecoxib Integrated Safety vs Ibuprofen or Naproxen (PRECISION) trial was conducted to address the remaining concerns about the relative cardiovascular safety of COX-2 selective NSAIDs and nonselective NSAIDs. PRECISION was a large, randomized, double-blind controlled trial that began in 2006. Ninety percent of the patients enrolled in the trial had osteoarthritis, and the remaining 10% had rheumatoid arthritis.

Results of the PRECISION trial demonstrated that celecoxib at the lowest approved dose of 100 mg twice daily is noninferior to (or no worse than) ibuprofen dosed in the range of 600 mg to 800 mg three times daily or naproxen dosed in the range of 375 mg to 500 mg twice daily on a composite cardiovascular endpoint consisting of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke.

In an ambulatory blood pressure monitoring study that was part of the larger PRECISION trial, celecoxib dosed at 100 mg twice daily showed little effect on average 24-hour systolic blood pressure (SBP), whereas ibuprofen dosed in the range of 600 mg to 800 mg three times daily and naproxen dosed in the range of 375 mg to 500 mg twice daily increased average 24-hour SBP

**(Celebrex—Pfizer)**

**At lowest dose, CV safety similar to moderate doses of naproxen, ibuprofen**

by 3.7 mmHg and 1.6 mmHg, respectively.

Too few patients received higher doses of celecoxib to evaluate the risk of cardiovascular events or the effect on blood pressure for doses greater than 100 mg twice daily. The cardiovascular risks of the NSAID class are dose dependent; therefore, the results for celecoxib 100 mg twice daily on the composite cardiovascular endpoint and the lack of effect on SBP cannot be extrapolated to dosing regimens using the higher strengths of celecoxib (200 mg or 400 mg).

Patients with recent cardiovascular events such as acute MI, coronary revascularization, or coronary stent placement were not studied in the PRECISION trial. NSAID class labeling warns against use of NSAIDs in such patients.

**Source URL:**

<http://www.aphadruginfoline.com/alerts-and-recalls/lowest-dose-cv-safety-similar-moderate-doses-naproxen-ibuprofen>



## [Alerts and Recalls](#)

### Generic Name (Trade Name—Company)

July 9, 2018

### Neostigmine methylsulfate 5-mL syringes

**(No trade names—Fagron Sterile Services)**

**Two lots of recalled syringe units may be incorrectly labeled**

### Uses/Notes

Fagron Sterile Services is voluntarily [recalling two lots](#) of neostigmine methylsulfate 5-mL syringes because some syringe units containing 1 mg/mL, 5 mg per 5mL, are incorrectly labelled as 1 mg/mL, 3 mg per 3mL. Secondary packages are properly labelled as neostigmine methylsulfate 1 mg/mL, 5 mg per 5mL.

If 5 mL rather than the intended 3mL is administered to a patient, adverse events overdosage can range from nausea, vomiting, diarrhea, excessive salivation and sweating, increased bronchial secretions, miosis, bradycardia or tachycardia, cardiospasm, bronchospasm, incoordination, muscle cramps, fasciculation, and paralysis, to cholinergic crisis resulting in death.

To date, Fagron has not received any reports of adverse events or injuries related to this recall.

Neostigmine methylsulfate injection is a cholinesterase inhibitor indicated for reversal of the effects of nondepolarizing neuromuscular blocking agents after surgery.

### Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/two-lots-recalled-syringe-units-may-be-incorrectly-labeled>

## [Alerts and Recalls](#)

### Generic Name (Trade Name—Company)

July 9, 2018

### Kratom products

**(Blissful Remedies—World Organix LLC)**

**Recalled kratom products are contaminated with high counts of bacteria**

### Uses/Notes

[FDA is advising](#) consumers not to use kratom products sold by World Organix LLC, Las Vegas, NV. FDA laboratory analysis found that the products are contaminated with high counts of various bacteria that can cause infections, including salmonella, *Clostridium difficile*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*.

The products were [recalled](#) on June 30, 2018; however, FDA is concerned this recall does not include all lot numbers of the affected products.

FDA has received [reports of adverse events](#) associated with kratom products. The agency strongly discourages the public from consuming kratom, as there are no proven medical uses for kratom, an inherently addictive product that can cause harm.

### Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/recalled-kratom-products-are-contaminated-high-counts-bacteria>

## Supplemental Approvals

### Generic Name (Trade Name—Company)

July 9, 2018

### Encorafenib, binimetinib

**(Braftovi, Mektovi—Array BioPharma)**

**Agents approved in combination for unresectable or metastatic melanoma with BRAF mutations**

### Uses/Notes

FDA approved [encorafenib and binimetinib](#) in combination for patients with unresectable or metastatic melanoma with a *BRAF* V600E or V600K mutation, as detected by an FDA-approved test.

Approval was based on a randomized, active-controlled, open-label, multicenter trial in 577 patients with *BRAF* V600E or V600K mutation-positive unresectable or metastatic melanoma. Patients were randomized (1:1:1) to receive binimetinib 45 mg twice daily plus encorafenib 450 mg once daily, encorafenib 300 mg once daily, or vemurafenib 960 mg twice daily. Treatment continued until disease progression or unacceptable toxicity.

The major efficacy measure was progression-free survival (PFS) using RECIST 1.1 response criteria and assessed by blinded independent central review. The median PFS was 14.9 months for patients receiving binimetinib plus encorafenib and 7.3 months for the vemurafenib monotherapy arm (hazard ratio 0.54 [95% CI 0.41–0.71],  $P < 0.0001$ ). Overall response rates assessed by central review were 63% and 40%, respectively. Median response duration was 16.6 months vs. 12.3 months, respectively.

The most common (>25%) adverse reactions in patients receiving the combination were fatigue, nausea, diarrhea, vomiting, abdominal pain, and arthralgia. Discontinuation of therapy due to adverse reactions occurred in 5% of patients receiving the combination; the most common reasons were hemorrhage and headache.

FDA also granted approval of the THxID BRAF Kit (bioMérieux) as a companion diagnostic for these therapeutics.

The recommended doses are binimetinib 45 mg orally twice daily and encorafenib 450 mg orally once daily.

### Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/agents-approved-combination-unresectable-or-metastatic-melanoma-braf>

## [New Drug Approvals](#)

### Generic Name (Trade Name—Company)

July 9, 2018

### Glycopyrronium

**(Qbrexza—Dermira)**

**FDA approves first once-daily, topical prescription for excessive underarm sweating**

### Uses/Notes

Dermira announced FDA [approval of glycopyrronium](#) cloth, an anticholinergic indicated for topical treatment of primary axillary hyperhidrosis in adult and pediatric patients aged 9 years and older.

Commonly known as excessive underarm sweating, primary axillary hyperhidrosis is a chronic medical skin condition that results in sweating beyond what is needed for normal body temperature regulation. The exact cause is unknown, but it affects nearly 10 million people in the United States, with both men and women having similar prevalence. Approved under the trade name Qbrexza (pronounced kew brex' zah), it is applied directly to the skin and is designed to block sweat production by inhibiting sweat gland activation.

Approval was based on [results](#) from two Phase III clinical trials, ATMOS-1 and ATMOS-2, which evaluated the efficacy and safety of Qbrexza in patients with primary axillary hyperhidrosis. Both trials assessed the absolute change from baseline in sweat production (the weight or amount of sweat a patient produced) following treatment with Qbrexza and the proportion of patients who achieved at least a four-point improvement from baseline in their sweating severity, as measured by the Axillary Sweating Daily Diary (ASDD), Dermira's proprietary patient-reported outcome (PRO) instrument.

The most common adverse effects observed following topical application of Qbrexza to the underarms were dry mouth, dilated pupil, sore throat, headache, urinary hesitation, blurred vision, dry nose, dry throat, dry eye, dry skin, and constipation. The most common local skin reactions were erythema, burning/stinging, and pruritus.

Qbrexza is expected to be available nationwide in pharmacies beginning in October 2018. For more information, visit [www.qbrexza.com](http://www.qbrexza.com).

### Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-first-once-daily-topical-prescription-excessive-underarm-sweating>

## [Supplemental Approvals](#)

### Generic Name (Trade Name—Company)

July 9, 2018

### **Incobotulinumtoxin A**

***(Xeomin—Merz North America)***

**First neurotoxin approved for chronic sialorrhea, or excessive drooling**

### Uses/Notes

FDA approved [incobotulinumtoxinA](#) to treat chronic sialorrhea, or excessive drooling, in adult patients. It is the first and only neurotoxin with this approved indication in the United States.

Sialorrhea is a common symptom among patients who have neurological disorders such as Parkinson disease, amyotrophic lateral sclerosis, or cerebral palsy or who have had a stroke. The condition can occur from difficulty retaining saliva inside the mouth, from issues with swallowing, and from problems controlling facial muscles.

Approval for this indication was based on a Phase III, randomized, double-blind, placebo-controlled, multicenter trial involving 184 patients in which both coprimary endpoints were successfully achieved. Study participants received placebo (n = 36), incobotulinumtoxinA 75 U (n = 74), or incobotulinumtoxinA 100 U (n = 74). Overall frequency of adverse events was similar between placebo and treatment groups, with no new or unexpected adverse events reported.

This is the fourth neurological indication for the neurotoxin, which was first approved by FDA in 2010 to treat cervical dystonia and blepharospasm (in patients previously treated with onabotulinumtoxinA) in adult patients and later in 2015 for upper limb spasticity in adult patients.

### Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/first-neurotoxin-approved-chronic-sialorrhea-or-excessive-drooling>

## [New Drug Approvals](#)

### Generic Name (Trade Name—Company)

July 16, 2018

### **Tecovirimat**

**(Tpoxx—SIGA Technologies)**

**FDA approves first drug with an indication for treatment of smallpox**

### Uses/Notes

FDA has approved [tecovirimat](#), the first drug with an indication for treatment of smallpox. Though the World Health Organization declared smallpox, a contagious and sometimes fatal infectious disease, eradicated in 1980, there have been longstanding concerns that smallpox could be used as a bioweapon.

Prior to its eradication in 1980, variola virus, the virus that causes smallpox, was mainly spread by direct contact between people. Symptoms typically began 10 to 14 days after infection and included fever, exhaustion, headache, and backache. A rash initially consisting of small, pink bumps progressed to pus-filled sores before finally crusting over and scarring. Complications of smallpox could include encephalitis (inflammation of the brain), corneal ulcerations (an open sore on the clear, front surface of the eye) and blindness.

Tecovirimat's effectiveness against smallpox was established by studies conducted in animals infected with viruses that are closely related to the virus that causes smallpox and was based on measuring survival at the end of the studies. More animals treated with tecovirimat lived compared with the animals treated with placebo.

It was approved under the FDA's Animal Rule, which allows efficacy findings from adequate and well-controlled animal studies to support an FDA approval when it is not feasible or ethical to conduct efficacy trials in humans.

Safety of the agents was evaluated in 359 healthy human volunteers without a smallpox infection. The most frequently reported adverse effects were headache, nausea, and abdominal pain.

### Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-first-drug-indication-treatment-smallpox>

## Alerts and Recalls

### Generic Name (Trade Name—Company)

July 16, 2018

### Valsartan

### Uses/Notes

[FDA is alerting](#) health professionals and patients of a voluntary recall of several drug products containing the active ingredient valsartan, used to treat high blood pressure and heart failure. This recall is due to an impurity, N-nitrosodimethylamine (NDMA), which was found in the recalled products. However, not all products containing valsartan are being recalled. NDMA is classified as a probable human carcinogen based on results from laboratory tests. The presence of NDMA was unexpected and is thought to be related to changes in the way the active substance was manufactured.

FDA's review is ongoing and has included investigating the levels of NDMA in the recalled products, assessing the possible effect on patients who have been taking them and what measures can be taken to reduce or eliminate the impurity from future batches produced by the company.

Because valsartan is used in medicines to treat serious medical conditions, patients taking the recalled valsartan-containing medicines should continue taking their medicine until they have a replacement product. To determine whether a specific product has been recalled, patients should look at the drug name and company name on the label of their prescription bottle. If the information is not on the bottle, patients should contact the pharmacy that dispensed the medicine. If a patient is taking one of the recalled medicines, they should follow the recall instructions provided by the specific company. This information will be posted to the FDA's [website](#).

Patients should also contact their health professional (the pharmacist who dispensed the medication or doctor who prescribed the medication) if their medicine is included in this recall to discuss their treatment, which may include another valsartan product not affected by this recall or an alternative treatment option.

The companies listed are recalling all lots of nonexpired products that contain the ingredient valsartan supplied by a third party. Not all valsartan-containing medicines distributed in the United States have valsartan active pharmaceutical ingredient (API) supplied by this specific

***(Multiple trade names—Multiple companies)***

**FDA announces voluntary recall of several medicines containing valsartan following detection of an impurity**

company. The supplier has stopped distributing its valsartan API, and FDA is working with the affected companies to reduce or eliminate the valsartan API impurity from future products.

FDA will continue to investigate this issue and provide additional information when it becomes available.

**Source URL:**

<http://www.aphadruonline.com/alerts-and-recalls/fda-announces-voluntary-recall-several-medicines-containing-valsartan-following>

## Alerts and Recalls

### Generic Name (Trade Name—Company)

July 16, 2018

### Fluoroquinolone antibiotics

### Uses/Notes

[FDA is strengthening](#) the current warnings in the prescribing information that fluoroquinolone antibiotics may cause significant decreases in blood glucose and certain mental health adverse effects. The low blood glucose levels can result in serious problems, including coma, particularly in older people and patients with diabetes who are taking medications to reduce blood glucose levels.

The agency announced it is making these changes because a recent review found reports of life-threatening low blood glucose adverse effects and reports of additional mental health adverse effects.

FDA is requiring these updates in the [drug labels](#) and to the patient [Medication Guides](#) for the entire class of fluoroquinolones (see List of FDA-Approved Fluoroquinolones for Systemic Use). This affects only the fluoroquinolone formulations taken by mouth or given by injection. Blood glucose disturbances, including high blood and low blood glucose levels, are already included as a warning in most fluoroquinolone drug labels; however, FDA is adding that low blood glucose levels (hypoglycemia) can lead to coma.

Across the fluoroquinolone antibiotic class, a range of mental health adverse effects are already described under Central Nervous System Effects in the Warnings and Precautions section of the drug label, which differed by individual drug. The new label changes will make the mental health adverse effects more prominent and more consistent across the systemic fluoroquinolone drug class.

The mental health adverse effects to be added to or updated across all the fluoroquinolones are disturbances in attention, disorientation, agitation, nervousness, memory impairment, and serious disturbances in mental abilities (delirium).

Patients should tell their health professionals if they are taking a diabetes medicine when their health professional is considering prescribing an antibiotic, and also if they have low blood glucose or symptoms of it

**(Multiple trade names—Multiple companies)**

**FDA announces label changes, reissues warnings about fluoroquinolone antibiotics**

while taking a fluoroquinolone. Health professionals may ask patients with diabetes to check their blood glucose levels more often while taking a fluoroquinolone.

Health professionals should be aware of the potential risk of hypoglycemia sometimes resulting in coma, occurring more frequently in older adults and those with diabetes taking an oral hypoglycemic medicine or insulin. Alert patients of the symptoms of hypoglycemia, carefully monitor blood glucose levels in these patients, and discuss with them how to treat themselves if they have symptoms of hypoglycemia. Inform patients about the risk of psychiatric adverse reactions that can occur after just one dose.

Stop fluoroquinolone treatment immediately if a patient reports any central nervous system adverse effects, including psychiatric adverse reactions, or blood glucose disturbances, and switch to a nonfluoroquinolone antibiotic if possible. Stop fluoroquinolone treatment immediately if a patient reports serious adverse effects involving the tendons, muscles, joints, or nerves, and switch to a nonfluoroquinolone antibiotic to complete the patient's treatment course.

Health professionals should not prescribe fluoroquinolones to patients who have other treatment options for acute [bacterial sinusitis \(ABS\)](#), [acute bacterial exacerbation of chronic bronchitis \(ABECB\)](#), [and uncomplicated urinary tract infections \(uUTI\)](#) because the risks outweigh the benefits in these patients.

**Source URL:**

<http://www.aphadruginfo.com/alerts-and-recalls/fda-announces-label-changes-reissues-warnings-about-fluoroquinolone-antibiotics>

## Supplemental Approvals

### Generic Name (Trade Name—Company)

July 19, 2018

### Ribociclib

*(Kisqali—Novartis)*

### FDA expands use of breast cancer drug

### Uses/Notes

[FDA approved ribociclib](#) in combination with an aromatase inhibitor for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor (HR)–positive, human epidermal growth factor receptor 2 (HER2)–negative advanced or metastatic breast cancer, as initial endocrine-based therapy.

FDA also approved ribociclib in combination with fulvestrant for the treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine based therapy or following disease progression on endocrine therapy.

This is the first approval that FDA has granted as part of two new pilot programs announced earlier this year that collectively aim to make the development and review of cancer drugs more efficient, while improving FDA’s rigorous standard for evaluating efficacy and safety. With this real-time review, FDA was able to start evaluating the clinical data as soon as the trial results become available, enabling FDA to be ready to approve the new indication upon filing of a formal application with the agency.

Currently the two pilot programs are being used for supplemental applications for already approved cancer drugs and could later be expanded to original drugs and biologics.

Ribociclib was first approved in March 2017 for use with an AI to treat HR-positive, HER2-negative breast cancer in postmenopausal women whose cancer is advanced or has spread to other parts of the body.

### Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/fda-expands-use-breast-cancer-drug>

## [Supplemental Approvals](#)

### Generic Name (Trade Name—Company)

July 19, 2018

### **Darunavir, cobicistat, emtricitabine, tenofovir alafenamide**

**(Symtuza—Janssen)**

**First once-daily, darunavir-based single-tablet  
regimen approved for treatment of HIV 1 infection**

### Uses/Notes

[Janssen announced](#) FDA approval of darunavir 800 mg, cobicistat 150 mg, emtricitabine 200 mg, and tenofovir alafenamide 10 mg under the trade name Symtuza—the first and only complete, darunavir-based single-tablet regimen (STR) for the treatment of HIV-1 in treatment-naïve and certain virologically suppressed adults.

Symtuza combines the high barrier to resistance of darunavir with a formulation designed for improved tolerability and the convenience of an STR.

Approval was based on data from two 48-week, noninferiority, pivotal Phase III studies that assessed the safety and efficacy of Symtuza versus a control regimen in adults with no prior antiretroviral history (AMBER) and in virologically suppressed adults (EMERALD).

Results from both trials demonstrated that Symtuza was effective and well tolerated, with up to 95% achieving or maintaining virologic suppression (HIV-1 RNA < 50 c/mL).

The recommended dosage of Symtuza is one tablet taken once daily with food. Symtuza is not recommended in patients with creatinine clearance below 30 mL per minute or those with severe hepatic impairment.

According to the prescribing information, prior to or when initiating treatment with Symtuza, patients should be tested for hepatitis B virus (HBV) infection and renal function, and renal function should be monitored as clinically appropriate during therapy. The agent comes with a boxed warning on the risk of posttreatment acute exacerbation of hepatitis B.

### Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/first-once-daily-darunavir-based-single-tablet-regimen-approved-treatment-hiv>

## [New Drug Approvals](#)

### Generic Name (Trade Name—Company)

July 26, 2018

### Ivosidenib

### Uses/Notes

FDA [approved ivosidenib](#) tablets, the first drug in its class—[isocitrate dehydrogenase-1 inhibitor](#)—to treat relapsed or refractory acute myeloid leukemia (AML) in adults with a specific mutation in the IDH1 gene. The agency also approved the RealTime IDH1 Assay, a companion diagnostic used to detect IDH1 gene mutations.

The agent works by decreasing abnormal production of the oncometabolite 2-hydroxyglutarate (2-HG), leading to differentiation of malignant cells. If the IDH1 mutation is detected in blood or bone marrow samples using the RealTime IDH1 Assay, the patient may be eligible for treatment with ivosidenib.

Ivosidenib's efficacy was studied in a single-arm trial of 174 adult patients with relapsed or refractory AML with an IDH1 mutation. The trial measured the percentage of patients with no evidence of disease and full recovery of blood counts after treatment (complete remission, or CR), as well as patients with no evidence of disease and partial recovery of blood counts after treatment (complete remission with partial hematologic recovery, or CRh).

With a median follow-up of 8.3 months, 32.8% of patients experienced a CR orCRh that lasted a median 8.2 months. Of the 110 patients who required transfusions of blood or platelets due to AML at the start of the study, 37% went at least 56 days without requiring a transfusion after treatment with ivosidenib.

Common adverse effects are fatigue, increase in white blood cells, joint pain, diarrhea, shortness of breath, swelling in the arms or legs, nausea, pain or sores in the mouth or throat, irregular heartbeat (QT prolongation), rash, fever, cough, and constipation. Women who are breastfeeding should not take ivosidenib because it may cause harm to a newborn baby.

A boxed warning cautions that an adverse reaction known as differentiation syndrome can occur and can be fatal if not treated.

***(Tibsovo—Agiros Pharmaceuticals)***

**Drug is first to target relapsed or refractory AML in adults with IDH1 gene mutation**

Signs and symptoms of differentiation syndrome may include fever, difficulty breathing (dyspnea), acute respiratory distress, inflammation in the lungs (radiographic pulmonary infiltrates), fluid around the lungs or heart (pleural or pericardial effusions), rapid weight gain, swelling (peripheral edema) or liver (hepatic), kidney (renal) or multi-organ dysfunction.

At first suspicion of symptoms, health care providers should treat patients with corticosteroids and monitor patients closely until symptoms go away.

Other serious warnings include QT prolongation, which can be life threatening. Electrical activity of the heart should be tested with an electrocardiogram during treatment. Guillain-Barré syndrome also has occurred with treatment, so patients should be monitored for nervous system problems.

Ivosidenib must be dispensed with a patient Medication Guide that describes important information about the drug's uses and risks.

**Source URL:**

<http://www.aphadruginfoline.com/new-drug-approvals/drug-first-target-relapsed-or-refractory-aml-adults-idh1-gene-mutation>

## [New Drug Approvals](#)

### Generic Name (Trade Name—Company)

July 26, 2018

### **Filgrastim-aafi**

**(Nivestym—Pfizer)**

**FDA approves Nivestym, second biosimilar to Neupogen**

### Uses/Notes

FDA has approved [filgrastim-aafi](#), a biosimilar to Neupogen (filgrastim), under the trade name Nivestym.

Approval was based on a review of a comprehensive data package and totality of evidence demonstrating a high degree of similarity of Nivestym compared to its reference product.

In the United States, it is indicated for the following: to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever; to reduce the time to neutrophil recovery and duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML); to reduce the duration of neutropenia and neutropenia-related clinical sequelae (e.g., febrile neutropenia) in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT); for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis; and for chronic administration to reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Common adverse effects include aching in the bones and muscles.

Serious risks include spleen enlargement and rupture, acute respiratory distress syndrome (ARDS), serious allergic reactions, sickle cell crises, and kidney injury.

### Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-nivestym-second-biosimilar-neupogen>

## [New Drug Approvals](#)

### Generic Name (Trade Name—Company)

July 26, 2018

### Tafenoquine

**(Krintafel—GSK and Medicines for Malaria Venture)**

**FDA approves new drug for radical cure of *P. vivax* malaria**

### Uses/Notes

GSK and Medicines for Malaria Venture [announced](#) FDA approval of single-dose tafenoquine for the radical cure (prevention of relapse) of *Plasmodium vivax* malaria in patients aged 16 years and older who are receiving appropriate antimalarial therapy for acute *P. vivax* infection.

Tafenoquine is an 8-aminoquinoline derivative with activity against all stages of the *P. vivax* life cycle, including hypnozoites. It was first synthesised by scientists at the Walter Reed Army Institute of Research in 1978.

Approval was based on efficacy and safety data from a comprehensive global clinical development *P. vivax* radical cure program designed in agreement with FDA. Thirteen studies in healthy volunteers and patients directly supported the program.

The primary evidence for clinical efficacy and safety of the 300-mg single dose was provided by three randomized, double-blind studies: DETECTIVE Part 1 and Part 2 (TAF112582) and GATHER (TAF116564) involving 800 participants. Results of the two Phase III studies were announced in June 2017. The submission included data analyzed from 33 studies involving more than 4,000 trial participants treated with the 300-mg single-dose and other doses of tafenoquine.

The most common adverse reactions (5%) observed in clinical trials were dizziness, nausea, vomiting, headache, and decreased hemoglobin.

### Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-new-drug-radical-cure-p-vivax-malaria>

## [New Drug Approvals](#)

### Generic Name (Trade Name—Company)

July 26, 2018

### Elagolix

### Uses/Notes

[Abbvie announced](#) FDA approval of elagolix, the first and only oral gonadotropin-releasing hormone (GnRH) antagonist specifically developed for women with moderate to severe endometriosis pain—and the first FDA-approved oral treatment for this condition in more than a decade.

Endometriosis-associated pain is often managed with medications such as oral contraceptives, NSAIDs, opioids, and hormonal therapies. These treatments can work for some women, but very few are specifically indicated for treatment of endometriosis. In more extensive cases of the disease, surgical interventions (e.g., laparotomy, laparoscopy, or hysterectomy) are often pursued and may not be curative for all individuals.

Approval was supported by data from two replicate studies in the largest endometriosis Phase III study program conducted to date, which evaluated nearly 1,700 women with moderate to severe endometriosis pain.

Clinical trial data demonstrated that elagolix significantly reduced the three most common types of endometriosis pain: daily menstrual pelvic pain, nonmenstrual pelvic pain, and pain with sex. A higher proportion of women treated with elagolix 150 mg once daily and 200 mg twice daily were responders for daily menstrual pain and nonmenstrual pelvic pain compared with placebo in a dose-dependent manner at month three. Women were defined as responders if they experienced a reduction in daily menstrual pain and nonmenstrual pelvic pain with no increase in analgesic use (NSAID or opioid) for endometriosis-associated pain.

Both elagolix treatment groups showed statistically significant greater mean decreases from baseline compared with placebo in daily menstrual pain and nonmenstrual pelvic pain at month six. Women in the Phase III studies also provided a daily self-assessment of their endometriosis pain using a numeric rating scale (NRS). Women taking elagolix 150 mg once daily and 200 mg twice daily reported a statistically ( $P < 0.001$ ) significant reduction from baseline in NRS scores

**(Orilissa—Abbvie)**

**New drug is first oral treatment in a decade for endometriosis pain**

compared with placebo at month three.

Data also demonstrated that women taking elagolix 200 mg twice daily showed statistically significant greater reduction in pain with sex from baseline to month three compared with placebo.

The recommended duration of use for elagolix is up to 24 months for the 150 mg once daily dose and up to 6 months for the 200 mg twice daily dose, as it causes a dose-dependent decrease in bone mineral density (BMD). BMD loss is greater with increasing duration of use and may not be completely reversible after stopping treatment.

For women with moderate hepatic impairment, the recommended dosage is 150 mg once daily for up to 6 months.

Elagolix is recommended to be taken orally at approximately the same time each day, with or without food. The new agent is expected to be available in U.S. pharmacies in early August 2018.

**Source URL:**

<http://www.aphadruginfoline.com/new-drug-approvals/new-drug-first-oral-treatment-decade-endometriosis-pain>

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