
A^{PhA} **DrugInfoLine[®]**

March 2019

[Focus on HIV Care](#)

Advising on this article: Betty J. Dong

March 4, 2019

Hospitalizations common in patients with HIV receiving contraindicated interacting medications

Key Point

A higher proportion of persons with HIV starting antiretroviral therapy (ART) and receiving contraindicated coadministered medications were hospitalized within the first year compared with those not receiving interacting medications, according to an observational study published in *AIDS Research and Human Retroviruses*.

Source URL:

<http://www.aphadruginfoline.com/focus-hiv-care/hospitalizations-common-patients-hiv-receiving-contraindicated-interacting>

[Neurology](#)

Advising on this article: Jack J. Chen

March 4, 2019

Rituximab an option for secondary progressive MS

Key Point

Patients with secondary progressive multiple sclerosis (MS), an advanced form of MS, who were treated with rituximab had significantly lower scores on the Expanded Disability Status Scale (EDSS) and a significantly delayed time to confirmed progression compared with patients not given rituximab, according to results of an observational study published in JAMA Neurology.

Source URL:

<http://www.aphadruginfoline.com/neurology/rituximab-option-secondary-progressive-ms>

[Infectious Diseases](#)

Advising on this article: Allana Sucher

March 12, 2019

IDSA releases updated influenza guidelines

Key Point

The Infectious Diseases Society of America (IDSA) released updated guidance on management of seasonal influenza, including information on diagnostic testing, antiviral treatments, chemoprophylaxis, and institutional outbreaks.

Source URL:

<http://www.aphadruginfoline.com/infectious-diseases/idsa-releases-updated-influenza-guidelines>

Cardiology

Advising on this article: Eric MacLaughlin

March 12, 2019

Intensive BP control may reduce the risk of mild cognitive impairment

Key Point

Treatment of hypertension to systolic blood pressure (SBP) levels of less than 120 mm Hg did not result in a lower incidence of dementia, but did significantly reduce the risk of mild cognitive impairment compared with less-intensive BP control to SBP levels of less than 140 mm Hg, according to data from the SPRINT MIND trial published in JAMA.

Source URL:

<http://www.aphadruginfoline.com/cardiology/intensive-bp-control-may-reduce-risk-mild-cognitive-impairment>

[Endocrinology](#)

Advising on this article: Frank Pucino

March 18, 2019

Testosterone use remains common in men with CAD despite risks

Key Point

Off-label use of testosterone remains high, including an increased use in men with coronary artery disease (CAD) compared with those without, according to an observational analysis that assessed trends in testosterone prescribing more than 10 years published in JAMA Internal Medicine.

Source URL:

<http://www.aphadruonline.com/endocrinology/testosterone-use-remains-common-men-cad-despite-risks>

[Nephrology](#)

Advising on this article:

March 18, 2019

Muscle relaxant use among hemodialysis patients is associated with adverse outcomes

Key Point

Use of muscle relaxants in patients receiving hemodialysis may alter mental status and increase the risk of falls, according to results of an observational cohort study published in the American Journal of Kidney Diseases.

Source URL:

<http://www.aphadruginfoline.com/nephrology/muscle-relaxant-use-among-hemodialysis-patients-associated-adverse-outcomes>

[OTC Medicines Corner](#)

Advising on this article: Tara Whetsel

March 26, 2019

E-cigarettes outperformed nicotine-replacement therapy for smoking cessation

Key Point

One-year abstinence rates were significantly higher in people who smoked who were randomized to e-cigarettes compared with those given nicotine-replacement therapies (NRTs), according to results of a multicenter study published in the New England Journal of Medicine.

Source URL:

<http://www.aphadruginfoline.com/otc-medicines-corner/e-cigarettes-outperformed-nicotine-replacement-therapy-smoking-cessation>

[Respiratory](#)

Advising on this article:

March 26, 2019

Beta-blocker use is associated with fewer COPD hospitalizations and deaths

Key Point

Data from a large Danish population-based study showed that treatment with beta-blockers, regardless of their selectivity on bronchial tone, was associated with a reduced risk of chronic obstructive pulmonary disease (COPD) hospitalizations and death from COPD compared with use of other antihypertensive agents, according to a study published in *EClinicalMedicine*.

Source URL:

<http://www.aphadruginfoline.com/respiratory/beta-blocker-use-associated-fewer-copd-hospitalizations-and-deaths>

Supplemental Approvals

Generic Name (Trade Name—Company)

March 5, 2019

Guselkumab

(Tremfya One-Press—Janssen)

Single-dose, patient-controlled injector approved for adults with moderate to severe plaque psoriasis

Uses/Notes

[Janssen announced](https://www.janssen.com/janssen-announces-us-fda-approval-novel-tremfya-guselkumab-one-press-patient-controlled-injector) FDA approval of guselkumab (Tremfya One-Press) as a single-dose, patient-controlled injector for adults with moderate to severe plaque psoriasis. Guselkumab is a human monoclonal antibody that selectively blocks the protein interleukin (IL)-23. Tremfya One-Press is administered as a 100-mg S.C. injection once every 8 weeks after starter doses at weeks 0 and 4. It is intended for use under the guidance and supervision of a physician, but patients may self-inject after physician approval and proper training. The injector fits comfortably in the hand and offers a controlled injection that hides the needle throughout the process, stated Janssen in a news release. The device allows patients to control the rate and pressure of their injection. A soft click indicates when administration is complete, and a safety system protects the needle after use. The most common adverse effects are upper respiratory infections, headache, injection-site reactions, joint pain, diarrhea, gastroenteritis, fungal skin infections, and herpes simplex infections.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/single-dose-patient-controlled-injector-approved-adults-moderate-severe>

Supplemental Approvals

Generic Name (Trade Name—Company)

March 5, 2019

Colchicine oral solution

(Gloperba—ROMEG Therapeutics)

FDA approves liquid formulation of colchicine for prophylaxis of gout flares

Uses/Notes

<p>FDA approved colchicine oral solution, 0.6 mg/5 mL, for prophylaxis of gout flares in adults.</p>

<p>Physicians have used colchicine to treat gout for decades, but they are often required to adjust the dose or interrupt treatment to address drug interactions or health conditions such as when patients are undergoing kidney dialysis. Compared with currently available capsule and tablet formulations of colchicine, the oral solution allows health care providers to easily make dosage adjustments for their patients, the manufacturer stated in a news release. The oral solution is also beneficial for patients who cannot swallow solid doses or pills. About 15% of older adult patients have difficulty swallowing and therefore require liquid formulations.</p> <p>The new formulation will be available in summer 2019.</p>

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-liquid-formulation-colchicine-prophylaxis-gout-flares>

Supplemental Approvals

Generic Name (Trade Name—Company)

March 5, 2019

Methylphenidate hydrochloride XR **(*Adhansia XR—Adlon Therapeutics*)**

Extended-release methylphenidate capsules approved for ADHD treatment

Uses/Notes

Methylphenidate hydrochloride extended-release (XR) capsules CII, a central nervous system stimulant, offers a methylphenidate treatment option with a longer duration of efficacy in patients with ADHD aged 6 years and older. The product will be available in six capsule strengths: 25, 35, 45, 55, 70, and 85 mg. The recommended starting dose is 25 mg taken orally once daily in the morning, with or without food. The dose should be titrated in increments of 10 mg to 15 mg at intervals of no less than 5 days. Capsules may be taken whole or opened and the entire contents sprinkled onto a tablespoon of applesauce or yogurt. The most common adverse reactions in adults are insomnia, dry mouth, and decreased appetite; in pediatric patients, they are decreased appetite, insomnia, and decreased weight. The prescribing information contains a boxed warning for abuse and dependence. Health professionals should assess the risk of abuse before prescribing the drug and monitor patients for signs of abuse and dependence. The drug is contraindicated in patients with a known hypersensitivity to methylphenidate or product components, as well as patients receiving concurrent treatment with a MAOI or those who have used an MAOI within the preceding 14 days.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/extended-release-methylphenidate-capsules-approved-adhd-treatment>

New Drug Approvals

Generic Name (Trade Name—Company)

March 6, 2019

Esketamine nasal spray

Uses/Notes

FDA has approved esketamine nasal spray, in conjunction with an oral antidepressant, to treat depression in adults who have not benefited from other antidepressants. Esketamine is the s-enantiomer of ketamine ([Ketalar] approved in 1970), which is a mixture of two enantiomers (mirror-image molecules). This is the first FDA approval of esketamine for any use.

Because of the potential for serious adverse outcomes resulting from sedation and dissociation, the drug will be available only through a restricted distribution system under a Risk Evaluation and Mitigation Strategy (REMS). Esketamine must also be dispensed with a patient Medication Guide that outlines the drug's uses and risks.

Patients self-administer esketamine nasal spray under the supervision of a health care provider in a certified doctor's office or clinic, and the spray cannot be taken home. The health care provider instructs the patient on how to operate the nasal spray device. During and after each use of the nasal spray device, the health care provider will check the patient and determine when the patient is ready to leave. Patients must be monitored by a health care provider for at least 2 hours after receiving their esketamine dose.

Efficacy of esketamine was evaluated in three short-term (4-week) clinical trials and one longer-term maintenance-of-effect trial. In the three short-term studies, patients were randomized to receive esketamine or a placebo nasal spray. In light of the serious nature of treatment-resistant depression and the need for patients to receive some form of treatment, all patients in these studies started a new oral antidepressant at the time of randomization, and the new antidepressant was continued throughout the trials. The primary efficacy measure was the change from baseline on a scale used to assess the severity of depressive symptoms.

In one of the short-term studies, esketamine nasal spray demonstrated statistically significant effect compared with placebo on

(Spravato—Janssen)

FDA approves new nasal spray medication for treatment-resistant depression

the severity of depression, and some effect was seen within 2 days. The two other short-term trials did not meet the prespecified statistical tests for demonstrating effectiveness. In the longer-term maintenance-of-effect trial, patients in stable remission or with stable response who continued treatment with esketamine plus an oral antidepressant experienced a statistically significantly longer time to relapse of depressive symptoms than patients on placebo nasal spray plus an oral antidepressant.

The most common adverse effects in clinical trials were disassociation, dizziness, nausea, sedation, vertigo, decreased feeling or sensitivity, anxiety, lethargy, increased blood pressure, vomiting, and feeling drunk.

Patients with unstable or poorly controlled hypertension or preexisting aneurysmal vascular disorders may be at increased risk for adverse cardiovascular or cerebrovascular effects. Esketamine may impair attention, judgment, thinking, reaction speed, and motor skills. Patients should not drive or operate machinery until the next day after a restful sleep. Because the drug may cause fetal harm, women of reproductive potential should consider pregnancy planning and prevention, and women should not breastfeed while being treated.

FDA granted this drug application [Fast Track](https://www.fda.gov/ForPatients/Approvals/Fast/ucm405399.htm) and [Breakthrough Therapy](https://www.fda.gov/ForPatients/Approvals/Fast/ucm405397.htm) designations.

Source URL:

<http://www.aphadruginfo.com/new-drug-approvals/fda-approves-new-nasal-spray-medication-treatment-resistant-depression>

Supplemental Approvals

Generic Name (Trade Name—Company)

March 6, 2019

Aprepitant injectable emulsion

(Cinvanti—Heron Therapeutics)

FDA expands approval of aprepitant as 2-minute I.V. injection

Uses/Notes

<p>Heron Therapeutics announced FDA approval of aprepitant injectable emulsion beyond the previous administration method (a 30-minute I.V. infusion) to include a 2-minute I.V. injection for prevention of acute and delayed chemotherapy-induced nausea and vomiting (CINV) in adults. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent substance P/neurokinin-1 receptor antagonist to significantly reduce CINV in both the acute phase (0–24 h after chemotherapy) and the delayed phase (24–120 h after chemotherapy).</p>
<p>The recommended dosage for I.V. injection following highly emetogenic cancer chemotherapy (single-dose regimen) is 130 mg on day 1. Following moderately emetogenic cancer chemotherapy (3-day regimen), the dosage is 100 mg on day 1, with aprepitant 80 mg capsules given orally on days 2 and 3. Treatment with the agent is part of a regimen that includes a corticosteroid and a 5-hydroxytryptamine receptor antagonist.</p>
<p>The most common adverse reactions with the 3-day oral aprepitant regimen in conjunction with MEC were fatigue and eructation. The most common adverse reactions with the single-dose I.V. fosaprepitant regimen in conjunction with HEC were generally similar to that seen in prior HEC studies with oral aprepitant. Infusion-site reactions also occurred.</p>
<p>The most common adverse reactions with single-dose aprepitant were headache and fatigue. The safety profile of aprepitant in healthy participants who received a single 2-minute injection was similar to that seen with a 30-minute infusion.</p>

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/fda-expands-approval-aprepitant-2-minute-iv-injection>

Supplemental Approvals

Generic Name (Trade Name—Company)

March 13, 2019

Valsartan

(No trade name—Alkem Laboratories Limited)

FDA approves a new generic valsartan

Uses/Notes

FDA approved a new https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm633255.htm?utm_campaign=FDA%20approves%20a%20new%20generic%20valsartan&utm_medium=email&utm_source=Eloqua generic valsartan in response to a recent shortage resulting from multiple recalls of generic valsartan products from several manufacturers after certain lots of valsartan and other ARB medicines were found to contain nitrosamine impurities. The agency is also working closely with manufacturers to see if they can produce additional supplies of these medications. FDA scientists are using the information learned from an investigation to evaluate all ARBs currently on the market and will also apply this information when assessing future applications to ensure that the manufacturing process can't form these impurities. For this approval, FDA evaluated the company's manufacturing processes and also made sure they used appropriate testing methods to demonstrate that the new generic valsartan does not contain NDMA or NDEA. FDA's assessment of the manufacturing processes for the product determined that there is no known risk for the formation of other nitrosamine impurities. FDA continues to investigate ARB medicines that contain nitrosamine impurities and that do not meet the agency's quality standards. The agency will continue to update the lists on its website of recalled valsartan, losartan, and irbesartan products as more information becomes available from ongoing testing. If patients take an ARB drug product, they should check the lists periodically, as information may change. Not all ARB medicines have been recalled. Valsartan treats high blood pressure and heart failure. Its most common adverse effects are dizziness, hypotension, hyperkalemia, and increased blood creatinine.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-new-generic-valsartan>

Supplemental Approvals

Generic Name (Trade Name—Company)

March 13, 2019

Trastuzumab-qyyp

(Trazimera—Pfizer)

FDA approves biosimilar to trastuzumab

Uses/Notes

https://www.pfizer.com/news/press-release/press-release-detail/u_s_fda_approves_pfizer_s_oncology_biosimilar_trazimera_trastuzumab_qyyp_a_biosimilar_to_herceptin_1 Pfizer announced FDA approval of trastuzumab-qyyp, a biosimilar to trastuzumab (Herceptin), for treatment of human epidermal growth factor receptor-2 (HER2) overexpressing breast cancer and HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

Approval was based on review of a comprehensive data package, which demonstrated a high degree of similarity between trastuzumab-qyyp and trastuzumab. This includes results from the REFLECTIONS B327-02 clinical comparative study recently published in the *British Journal of Cancer*, which showed clinical equivalence, finding a high degree of similarity and no clinically meaningful differences between trastuzumab and the originator product in patients with first-line, HER2-overexpressing metastatic breast cancer.

Trastuzumab is a monoclonal antibody biosimilar that targets HER2, a protein found on the surface of some cancer cells that can stimulate the cells to divide and grow. The agent locks on to the HER2 protein and blocks the receptors, stopping cell division and growth.

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-biosimilar-trastuzumab>

Supplemental Approvals

Generic Name (Trade Name—Company)

March 13, 2019

Atezolizumab

(Tecentriq—Roche)

Accelerated approval granted for treatment of triple-negative breast cancer

Uses/Notes

<p>FDA granted accelerated approval to atezolizumab plus chemotherapy (nab-paclitaxel [Abraxane]) for treatment of adults with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1, as determined by an FDA-approved test.</p> <p>Accelerated approval was based on data from a Phase III study demonstrating that atezolizumab plus nab-paclitaxel significantly reduced the risk of disease worsening or death by 40% compared with nab-paclitaxel alone in PD-L1-positive patients with unresectable locally advanced or metastatic TNBC who had not received prior chemotherapy for metastatic disease. </p> <p>The most common adverse effects of atezolizumab plus nab-paclitaxel were low white blood cell count, tingling or numbness in the hands and feet, decreased neutrophil count, fatigue, low red blood cell count, low blood potassium levels, pneumonia, and increased AST levels.</p>

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/accelerated-approval-granted-treatment-triple-negative-breast-cancer>

Supplemental Approvals

Generic Name (Trade Name—Company)

March 13, 2019

Dupilumab

(Dupixent—Regeneron/Sanofi)

Eczema drug has new indication for patients aged 12 to 17

Uses/Notes

<p><org idsrc="xmltag.org" value="REGN">Regeneron </org>and <org idsrc="xmltag.org" value="SNY">Sanofi</org> announced <org>FDA</org> <org>approval of dupilumab for patients aged 12 to 17 years with moderate to severe atopic dermatitis (eczema) whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids.</p> <p>The agent is a targeted biologic therapy that inhibits signaling of interleukin-4 (IL-4) and interleukin-13 (IL-13), two key proteins that may play a central role in type 2 inflammation that underlies atopic dermatitis and several other allergic diseases.</p> <p>Dupixent has been studied in more than 7,000 patients aged 12 years and older in more than 30 clinical trials. Its safety profile in the adolescent trial was similar to the safety profile from trials in adults with atopic dermatitis and consistent through 52 weeks.

 The most common adverse events were injection-site reactions; eye and eyelid inflammation, including redness, swelling; and itching; oropharyngeal pain; and cold sores in the mouth or on the lips.</p> <p>Dupixent comes in two doses (200 mg and 300 mg), each as a prefilled syringe. Dupixent is intended for S.C. injection and is given every other week following an initial loading dose. It can be given in a clinic or, for convenience, at home by self-administration after training by a health professional.</p> <p>Dupixent is also approved for treatment of adult patients with moderate to severe atopic dermatitis that is not well controlled with topical prescription drugs or who cannot use topical therapies; and for use with other asthma medications for maintenance treatment of moderate to severe asthma in people aged 12 years and older whose asthma is not controlled with their current asthma medicines.</p>

Source URL:

<http://www.aphadruonline.com/supplemental-approvals/eczema-drug-has-new-indication-patients-aged-12-17>

Supplemental Approvals

Generic Name (Trade Name—Company)

March 13, 2019

Netarsudil and latanoprost ophthalmic solution

(Rocklatan—Aerie Pharmaceuticals)

Once-daily, fixed-dose combination reduces elevated intraocular pressure

Uses/Notes

[Aerie Pharmaceuticals](http://investors.aeriepharma.com/news-releases/news-release-details/aerie-pharmaceuticals-announces-us-fda-approval-rocklatan) announced FDA approval of netarsudil and latanoprost ophthalmic solution 0.02%/0.005% to reduce elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. The once-daily eyedrop is a fixed-dose combination of latanoprost, the most widely prescribed prostaglandin analog (PGA), and netarsudil, the active ingredient in netarsudil ophthalmic solution 0.02% (Rhopressa), a first-in-class Rho kinase (ROCK) inhibitor specifically designed to target the trabecular meshwork (the eye's principal drainage pathway). The diseased trabecular meshwork is considered to be the main cause of elevated IOP in open-angle glaucoma and ocular hypertension. Netarsudil works by restoring outflow through the trabecular meshwork, while latanoprost increases fluid outflow through a secondary mechanism known as the uveoscleral pathway. Approval was based on data from two Phase III registration trials, in which the agent achieved its primary 90-day efficacy endpoint as well as positive 12-month safety and efficacy results, demonstrating statistically superior IOP reduction over latanoprost and netarsudil at every measured timepoint. Treatment was associated with generally mild and tolerable ocular adverse events, with minimal systemic side effects. The most common ocular adverse event in controlled clinical studies was conjunctival hyperemia. Ninety percent of patients who experienced hyperemia reported it as mild, and 5% discontinued because of it. Other common ocular adverse effects were instillation-site pain, corneal verticillata, and conjunctival hemorrhage. Aerie plans to launch the new product in the United States in the second quarter of 2019.

Source URL:

<http://www.aphadruonline.com/supplemental-approvals/once-daily-fixed-dose-combination-reduces-elevated-intraocular-pressure>

Supplemental Approvals

Generic Name (Trade Name—Company)

March 19, 2019

Atezolizumab

(Tecentriq—Roche)

First new initial treatment option approved for people with ES-SCLC in more than 20 years

Uses/Notes

<p>Roche announced FDA approval of atezolizumab in combination with carboplatin and etoposide (chemotherapy) for first-line treatment of adults with extensive-stage small cell lung cancer (ES-SCLC).</p> <p>Atezolizumab is a monoclonal antibody designed to bind with the PD-L1 protein expressed on tumor cells and tumor-infiltrating immune cells, blocking its interactions with both PD-1 and B7.1 receptors. By inhibiting PD-L1, the drug may enable the activation of T cells.</p> <p>Approval was based on results from a Phase III study showing that atezolizumab in combination with chemotherapy helped people live significantly longer compared with chemotherapy alone (median overall survival =12.3 vs. 10.3 mo; hazard ratio [HR] = 0.70 [95% CI 0.54–0.91]; P = 0.0069) in the intention-to-treat population.</p> <p>The atezolizumab-based combination also significantly reduced the risk of disease worsening or death (progression-free survival [PFS]) compared with chemotherapy alone (PFS = 5.2 vs. 4.3 mo; HR = 0.77, 0.62–0.96; P = 0.017). Safety for the atezolizumab and chemotherapy combination appeared consistent with the known safety profile of atezolizumab.</p> <p>Atezolizumab is approved in combination with bevacizumab, paclitaxel, and carboplatin (chemotherapy) for first-line treatment of adults with metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations.</p> <p>It is also approved for treatment of adults with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for NSCLC harboring these aberrations before receiving atezolizumab.</p>

Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/first-new-initial-treatment-option-approved-people-es-sclc-more-20-years>

New Drug Approvals

Generic Name (Trade Name—Company)

March 27, 2019

Brexanolone

Uses/Notes

FDA [approved](https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm633919.htm) brexanolone injection for I.V. use for treatment of postpartum depression (PPD) in adult women. This is the first drug approved by FDA specifically for PPD.

Brexanolone will be available only through a restricted REMS Program that requires the drug to be administered by a health care provider in a certified health care facility. The REMS requires that patients be enrolled in the program prior to administration of the drug.

Brexanolone is administered as a continuous I.V. infusion over 60 hours (2.5 d). Because of the risk of serious harm from sudden loss of consciousness, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. While receiving the infusion, patients must be accompanied during interactions with their child(ren). The need for these steps is addressed in a boxed warning in the drug's prescribing information.

Patients will be counseled on the risks of brexanolone treatment and instructed that they must be monitored for these effects at a health care facility for the entire 60 hours of infusion. Patients should not drive, operate machinery, or do other dangerous activities until feelings of sleepiness from the treatment have completely gone away.

Brexanolone's effectiveness was shown in two clinical studies in participants who received a 60-hour continuous I.V. infusion of brexanolone or placebo and were then followed for 4 weeks. One study included patients with severe PPD, and the other included patients with moderate PPD. The primary measure in the study was the mean change from baseline in depressive symptoms as measured by a depression rating scale.

In both placebo-controlled studies, brexanolone demonstrated superiority to placebo in improvement of depressive symptoms at the end of the first infusion. The improvement in depression was also observed at the end of the 30-day follow-up period.

The most common adverse reactions reported by patients included sleepiness, dry mouth, loss of consciousness, and flushing. Health care providers should consider

(Zulresso—Sage Therapeutics)

FDA approves first treatment specifically for postpartum depression

changing the therapeutic regimen, including discontinuing brexanolone in patients whose PPD becomes worse or who experience emergent suicidal thoughts and behaviors.</p>

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-first-treatment-specifically-postpartum-depression>

New Drug Approvals

Generic Name (Trade Name—Company)

March 27, 2019

Solriamfetol

Uses/Notes

[Jazz Pharmaceuticals](https://investor.jazzpharma.com/news-releases/news-release-details/jazz-pharmaceuticals-announces-us-fda-approval-sunositm) announced FDA approval of solriamfetol to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA). It is the first dual-acting dopamine and norepinephrine reuptake inhibitor (DNRI) approved for this treatment. The once-daily drug is approved in doses of 75 mg and 150 mg for patients with narcolepsy and doses of 37.5 mg, 75 mg, and 150 mg for patients with OSA.

Approval of solriamfetol was based on data from the TONES Phase III clinical program, which included four randomized placebo-controlled studies that demonstrated the superiority of solriamfetol relative to placebo. The most common adverse reactions reported in both the narcolepsy and OSA study populations were headache, nausea, decreased appetite, and anxiety. Solriamfetol was evaluated in more than 900 adults with excessive daytime sleepiness associated with narcolepsy or OSA and was shown to maintain its effect relative to placebo after 6 months of use.

In 12 week clinical studies, approximately 68%–74% of people taking solriamfetol at the 75 mg dose and 78%–90% of people taking solriamfetol at the 150 mg dose reported improvement in their overall clinical condition, as assessed by the Patient Global Impression of Change scale.

Although the exact mechanism of action is unknown, the effects of solriamfetol are thought to be mediated through its activity as a DNRI.

In a news release, Jazz Pharmaceuticals cautioned that solriamfetol is not indicated to treat the underlying airway obstruction in OSA. Practitioners should ensure that the underlying airway obstruction is treated with continuous positive airway pressure (CPAP) for at least 1 month before initiating solriamfetol for excessive daytime sleepiness in OSA and continued

(Sunosi—Jazz Pharmaceuticals)

during treatment.</p>

New drug treats excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/new-drug-treats-excessive-daytime-sleepiness-associated-narcolepsy-or-obstructive>

New Drug Approvals

Generic Name (Trade Name—Company)

March 27, 2019

Siponimod

(Mayzent—Novartis)

FDA approves first oral drug for relapsing forms of MS

Uses/Notes

FDA has approved [siponimod](https://www.novartis.com/news/media-releases/novartis-receives-fda-approval-mayzent-siponimod-first-oral-drug-treat-secondary-progressive-ms-active-disease) for treatment of adults with relapsing forms of multiple sclerosis (MS), including secondary progressive multiple sclerosis (SPMS) with active disease, relapsing remitting multiple sclerosis, and clinically isolated syndrome. SPMS is a debilitating form of MS characterized by progressive and irreversible neurological disability. Patients will not require a first dose observation (cardiac monitoring upon initiation) unless they have certain preexisting cardiac conditions. Approval was based on groundbreaking data from the Phase III EXPAND study, a randomized, double-blind, placebo-controlled study comparing the efficacy and safety of siponimod versus placebo in people living with SPMS. Patients enrolled in EXPAND were representative of a typical SPMS population. At study initiation, patients had a mean age of 48 years and had been living with MS for approximately 16 years. More than 50% had a median Expanded Disability Status Scale score of 6.0 and relied on a walking aid. Siponimod significantly reduced the risk of 3-month confirmed disability progression (CDP), meaningfully delayed the risk of 6-month CDP, and reduced the annualized relapse rate by 55%. Furthermore, EXPAND showed significant favorable outcomes in other relevant measures of MS disease activity, including cognition, MRI disease activity, and brain volume loss. The most common adverse reactions (incidence >10%) were headache, hypertension, and transaminase increase.

Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-first-oral-drug-relapsing-forms-ms>

Alerts and Recalls

Generic Name (Trade Name—Company)

March 27, 2019

Levoleucovorin injection

(No trade name—Mylan Institutional)

Two lots of levoleucovorin injection recalled

Uses/Notes

https://www.fda.gov/Safety/Recalls/ucm633784.htm?utm_campaign=FDA%20MedWatch%20Levoleucovorin%20Injection%20by%20Mylan%20Institutional&utm_medium=email&utm_source=Eloqua conducting a voluntary nationwide recall of two lots of levoleucovorin injection (#67457-601-30 and #67457-601-30), 250 mg/25 mL, to the consumer/user level. The lots, manufactured by Alidac Pharmaceuticals and distributed by Mylan, contain particulate matter identified as copper salts. The particulate matter was discovered during 12-month stability testing.

I.V. administration of a solution containing particulates could lead to local irritation, vasculitis/phlebitis, antigenic or allergic reactions, and microvascular obstruction, including pulmonary embolism.

Levoleucovorin injection is indicated for rescue after high-dose methotrexate therapy in osteosarcoma; for diminishing the toxicity and counteracting the effects of impaired methotrexate elimination and of inadvertent overdose of folic acid antagonists; and for use in combination chemotherapy with 5-fluorouracil in the palliative treatment of patients with advanced metastatic colorectal cancer.

Levoleucovorin injection 250 mg contains 25-mL sterile solution in a single-use vial. Each vial is packaged in a carton containing one single-use vial. The batches were distributed in the United States between August 2017 and July 2018.

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

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/two-lots-levoleucovorin-injection-recalled>

[Alerts and Recalls](#)

Generic Name (Trade Name—Company)

March 27, 2019

Dietary supplement

(Blue Fusion—Ata Int. Inc.)

Recalled Blue Fusion dietary supplement contains undeclared active ingredients

Uses/Notes

<p>Ata Int. Inc. is voluntarily recalling all lots within expiry of Blue Fusion capsules because the product is tainted with sildenafil, tadalafil, desmethyl carbodenafil, dithiodesmethyl carbodenafil, scutellarin, and daidzein.

 Sildenafil and tadalafil are FDA-approved drugs for treatment of male erectile dysfunction and are phosphodiesterase (PDE-5) inhibitors. Desmethyl carbodenafil and dithiodesmethyl carbodenafil are analogues of PDE-5 inhibitors and are likely to have the same pharmacological activity as PDE-5 inhibitors and thus carry the same clinical risks. Scutellarin and daidzein are derived from plants or herbs.</p> <p>Presence of the undeclared active ingredients renders the product an unapproved drug for which safety and efficacy have not been established; therefore, the product is subject to recall.</p> <p>Consumption of a product with undeclared PDE-5 inhibitors may pose a threat because the active ingredients may interact with nitrates found in some prescription drugs (such as nitroglycerin) and may lower blood pressure to dangerous levels, which can be life threatening. Patients with diabetes, high blood pressure, high cholesterol, or heart disease often take nitrates and may be the population most likely to be affected. </p> <p>Blue Fusion capsules were marketed as a dietary supplement for male enhancement and are packaged in 1-count blister packs (UPC code – 7.48252. 66460.0). The product was distributed nationwide between January 2015 and March 2019 to retail stores and through the internet.</p> <p>To date, Ata Int. Inc. has not received any reports of adverse events related to this recall.</p>

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/recalled-blue-fusion-dietary-supplement-contains-undeclared-active-ingredients>

Alerts and Recalls

Generic Name (Trade Name—Company)

March 27, 2019

Venetoclax

(Venclexta—AbbVie, Genentech)

FDA warns of risks associated with investigational use of venetoclax in multiple myeloma

Uses/Notes

FDA is alerting health professionals, oncology clinical investigators, and patients about the risks associated with the investigational use of venetoclax for treatment of patients with multiple myeloma. The agent is not approved for treatment of multiple myeloma.

FDA reviewed data from the BELLINI clinical trial evaluating the use of venetoclax combined with bortezomib, a proteasome inhibitor, and dexamethasone in patients with multiple myeloma. The interim trial results demonstrated an increased risk of death for patients receiving venetoclax, compared with the control group. On March 6, 2019, FDA required that no new patients be enrolled in the trial. Patients who are receiving clinical benefit can continue treatment in the trial after they re consent.

This statement does not apply to patients taking venetoclax for an approved indication, who should continue to take their medication as directed by their health professional. Venetoclax is safe and effective for its approved uses.

FDA suspended enrollment in other ongoing multiple myeloma clinical trials of venetoclax. Patients who are receiving clinical benefit can continue treatment in these trials after they re consent.

FDA said it will be working directly with sponsors of venetoclax, as well as other investigators conducting clinical trials in patients with multiple myeloma, to determine the extent of the safety issue. The agency will communicate any new information as appropriate.

Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/fda-warns-risks-associated-investigational-use-venetoclax-multiple-myeloma>

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