

---

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

**May 2018**

## [Focus on Asthma Care](#)

Advising on this article: Devra K. Dang

**May 1, 2018**

# **Increasing inhaled glucocorticoid doses to prevent asthma exacerbations**

## **Key Point**

In children with moderate to severe persistent asthma, quintupling the inhaled corticosteroid (ICS) dose at early signs of loss of asthma control did not reduce the rate of severe asthma exacerbations; however, in adolescents and adults, quadrupling the ICS dose when asthma control started to deteriorate did result in fewer severe exacerbations in a small group of patients, according to two studies published in the New England Journal of Medicine.

## **Source URL:**

<http://www.aphadruginfoline.com/focus-asthma-care/increasing-inhaled-glucocorticoid-doses-prevent-asthma-exacerbations>

## [Respiratory](#)

Advising on this article: Roy A. Pleasants, II

**May 1, 2018**

# **Nebulized glycopyrrolate improved outcomes in patients with COPD**

## **Key Point**

Data from two Phase III trials showed that the SUN-101/eFlow product (Lonhala Magnair—Sunovion)—nebulized glycopyrrolate delivered through an electronic device—was well tolerated and resulted in improved lung function and patient-reported outcomes (PROs) in individuals with moderate to very severe chronic obstructive pulmonary disorder (COPD).

## **Source URL:**

<http://www.aphadruginfoline.com/respiratory/nebulized-glycopyrrolate-improved-outcomes-patients-copd>

## [Cardiology](#)

Advising on this article: Eric MacLaughlin

**May 7, 2018**

# **Pharmacist interventions at black barbershops effective at reducing BP**

## **Key Point**

Pharmacist-led interventions in black barbershops resulted in significantly greater blood pressure (BP) reductions in patrons with uncontrolled hypertension (HTN) compared with an intervention that focused on barbers encouraging their patrons to make healthy lifestyle modifications and see their doctors, according to results of a trial published in the New England Journal of Medicine.

## **Source URL:**

<http://www.aphadruginfoline.com/cardiology/pharmacist-interventions-black-barbershops-effective-reducing-bp>

## [Nephrology](#)

Advising on this article: Edward F. Foote

**May 7, 2018**

# **Balanced crystalloids may be preferred to I.V. saline**

## **Key Point**

Two large, single-center trials published in the *New England Journal of Medicine* comparing balanced crystalloid solutions with saline in both noncritically ill and critically ill adults found that use of balanced crystalloid solutions resulted in significant reductions in the risk of major adverse kidney events within 30 days (defined as a composite of death from any cause, use of new renal-replacement therapy, or persistent renal dysfunction).

## **Source URL:**

<http://www.aphadruginfoline.com/nephrology/balanced-crystalloids-may-be-preferred-iv-saline>

## [Drug Interactions Corner](#)

Advising on this article: Daniel S. Streetman

**May 14, 2018**

# **Common antibiotics do not appear to interact with hormonal contraceptives**

## **Key Point**

Clinical and pharmacokinetic studies do not appear to support an interaction between hormonal contraceptives (HCs) and most nonrifamycin antibiotics (e.g., penicillins/cephalosporins, tetracyclines, fluoroquinolones, macrolides, and others), according to results of a systematic review of 29 studies published in the American Journal of Obstetrics and Gynecology.

## **Source URL:**

<http://www.aphadruginfoline.com/drug-interactions-corner/common-antibiotics-do-not-appear-interact-hormonal-contraceptives>

## [Infectious Diseases](#)

Advising on this article: Allana Sucher

**May 14, 2018**

# **Inappropriate use of antibiotics for acute sinusitis**

## **Key Point**

An observational study published in JAMA Internal Medicine that assessed more than 3 million physician office visits for acute sinusitis showed that more than two-thirds of prescribed antibiotics were given for 10 days or longer, despite current guidelines recommending a treatment duration of 5 to 7 days for uncomplicated cases in adult patients.

## **Source URL:**

<http://www.aphadruginfo.com/infectious-diseases/inappropriate-use-antibiotics-acute-sinusitis>

## Alerts and Recalls

### Generic Name (Trade Name—Company)

May 1, 2018

### Lamotrigine

### Uses/Notes

[FDA warned](#) that use of lamotrigine for seizures and bipolar disorder can cause a rare but very serious reaction that excessively activates the body's immune system. This can cause severe inflammation throughout the body and lead to hospitalization and death, especially if the reaction is not diagnosed and treated quickly. As a result, FDA is requiring a new warning that this risk be added to the prescribing information in the lamotrigine drug labels.

The immune system reaction, called hemophagocytic lymphohistiocytosis (HLH), typically presents as a persistent fever, usually greater than 101°F. HLH can lead to severe problems with blood cells and organs throughout the body, such as the liver, kidneys, and lungs.

Lamotrigine is used alone or with other medications to treat seizures in patients aged 2 years and older. It may also be used as maintenance treatment in patients with bipolar disorder.

Health professionals should be aware that prompt recognition and early treatment is important for improving HLH outcomes and decreasing mortality. Diagnosis is often complicated, as early signs and symptoms such as fever and rash are not specific.

HLH may also be confused with other serious immune-related adverse reactions. Evaluate patients who develop fever or rash promptly, and discontinue lamotrigine if HLH or another serious immune-related adverse reaction is suspected and an alternative etiology for the signs and symptoms cannot be established.

Since lamotrigine's 1994 approval, FDA identified eight cases worldwide of confirmed or suspected HLH associated with the medication in children and adults. This number includes only reports submitted to FDA and found in the medical literature, so there are likely additional cases about FDA is unaware, according to the agency. FDA determined there was reasonable evidence that lamotrigine was the cause of HLH in these



**(Lamictal—GlaxoSmithKline)**

**FDA warns of serious immune system reaction with use of lamotrigine**

eight cases based on the timing of events and order in which they occurred. These patients required hospitalization and received drug and other medical treatments, with one dying.

A link to the full communication detailing specific information for health professionals and the complete Data Summary can be found at [www.fda.gov/DrugSafetyCommunications](http://www.fda.gov/DrugSafetyCommunications).

**Source URL:**

<http://www.aphadruginfoline.com/alerts-and-recalls/fda-warns-serious-immune-system-reaction-use-lamotrigine>

## [Supplemental Approvals](#)

### Generic Name (Trade Name—Company)

May 1, 2018

### Dabrafenib, trametinib

### Uses/Notes

[FDA granted regular approval](#) to dabrafenib and trametinib in combination for the adjuvant treatment of patients with melanoma with *BRAF V600E* or *V600K* mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.

Approval was based on COMBI-AD, an international, multicenter, randomized, double-blind, placebo-controlled trial in 870 patients with Stage III melanoma with *BRAF V600E* or *V600K* mutations, and pathologic involvement of regional lymph node(s). Patients were randomly allocated (1:1) to receive dabrafenib 150 mg twice daily in combination with trametinib 2 mg once daily or two placebos for up to 1 year.

The major efficacy outcome was relapse-free survival (RFS). RFS was defined as the time from randomization to disease recurrence (local, regional, or distant metastasis), new primary melanoma, or death from any cause, whichever occurred first as assessed by the investigator.

Patients who received the combination treatment had a statistically significant improvement in RFS compared with those receiving placebo. Patients in the combination arm experienced fewer recurrences/deaths at the time of data cutoff: 38% (n = 166), compared with 57% (n = 248) in the placebo arm (hazard ratio 0.47 [95% CI 0.39–0.58];  $P < 0.0001$ ). The estimated median RFS was not reached for patients who received the combination therapy, compared with 16.6 months (95% CI 12.7–22.1) for those receiving placebo.

The most common adverse reactions in at least 20% of patients were pyrexia, fatigue, nausea, headache, rash, chills, diarrhea, vomiting, arthralgia, and myalgia.

Adverse reactions resulting in discontinuation, dose reduction, or dose interruption of dabrafenib occurred in 25%, 35%, and 66% of patients, respectively; the most common for each were pyrexia and chills.

**(Tafinlar, Mekinist—Novartis)**

**Dabrafenib plus trametinib approved for adjuvant treatment of melanoma with BRAF V600E or V600K mutations**

Adverse reactions resulting in discontinuation and dose interruption of trametinib occurred in 24% and 54% of patients respectively; the most common for each were pyrexia and chills.

Adverse reactions leading to dose reduction of trametinib occurred in 23% of patients; the most common were pyrexia and decreased ejection fraction.

The recommended doses for adjuvant treatment of melanoma are 150 mg of dabrafenib orally twice daily and 2 mg of trametinib orally once daily until disease recurrence or unacceptable toxicity, for up to 1 year.

**Source URL:**

<http://www.aphadruginfoline.com/supplemental-approvals/dabrafenib-plus-trametinib-approved-adjuvant-treatment-melanoma-braf-v600e-or>

## [Supplemental Approvals](#)

### Generic Name (Trade Name—Company)

May 1, 2018

### Tolvaptan

*(Jynarque—Otsuka)*

**Agent slows kidney function decline in adults at risk of rapidly progressing ADPKD**

### Uses/Notes

FDA has approved [tolvaptan](#) as the first drug treatment to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD), a genetic disease with consequences that can lead to dialysis or kidney transplantation.

ADPKD is a progressively debilitating and often painful disorder in which fluid-filled cysts develop in the kidneys over time. These cysts enlarge the kidneys and impair their ability to function normally, leading to kidney failure in most patients.

ADPKD is diagnosed in approximately 140,000 people in the United States and affects families across multiple generations, since a parent with ADPKD has a 50% chance of passing the disease on to each of their children.

Tolvaptan can cause serious and potentially fatal liver injury, and acute liver failure requiring liver transplantation has been reported. Tolvaptan has been associated with ALT and AST elevations, with infrequent cases of concomitant elevations in bilirubin-total.

To ensure the safety of patients taking tolvaptan, it is necessary to measure ALT, AST, and bilirubin before initiating treatment, at 2 weeks and 4 weeks after initiation, then monthly for 18 months and every 3 months thereafter, for as long as the patient is on tolvaptan treatment.

Because of the risks of serious liver injury, tolvaptan is available only through a restricted distribution program supported by a Risk Evaluation and Mitigation Strategy program approved by FDA.

### Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/agent-slows-kidney-function-decline-adults-risk-rapidly-progressing-adpkd>

## [Supplemental Approvals](#)

### Generic Name (Trade Name—Company)

May 7, 2018

### Dabrafenib, trametinib

### Uses/Notes

FDA [approved dabrafenib and trametinib](#), administered together, for treatment of anaplastic thyroid cancer (ATC) that cannot be removed by surgery or is metastatic and that is mutation positive for the *BRAF V600E* gene.

It is the first FDA-approved treatment for patients with this aggressive form of thyroid cancer, and the third cancer with this specific gene mutation that this drug combination has been approved to treat.

Both dabrafenib and trametinib are also approved for use, alone or in combination, to treat *BRAF V600* mutation-positive metastatic melanoma, and for use, in combination, to treat *BRAF V600E* mutation-positive, metastatic non–small cell lung cancer.

Efficacy of dabrafenib and trametinib in treating ATC was shown in an open-label clinical trial of patients with rare cancers with the *BRAF V600E* mutation. Data from trials in *BRAF V600E* mutation-positive, metastatic melanoma or lung cancer and results in other *BRAF V600E* mutation-positive rare cancers provided confidence in the results seen in patients with ATC.

The trial measured the percent of patients with a complete or partial reduction in tumor size (overall response rate). Of 23 evaluable patients, 57% experienced a partial response, and 4% experienced a complete response; in 9 (64%) of the 14 patients with responses, there were no significant tumor growths for 6 months or longer.

Adverse effects in patients with ATC are consistent with those seen in other cancers when the two drugs are used together. Common adverse effects include fever, rash, chills, headache, joint pain, cough, fatigue, nausea, vomiting, diarrhea, myalgia, dry skin, decreased appetite, edema, hemorrhage, hypertension, and difficulty breathing.

Adverse effects of dabrafenib include the development of new cancers, growth of tumors in patients with *BRAF* wild-type tumors, serious bleeding problems, heart

**(Tafinlar, Mekinist—Novartis)**

**FDA approves new uses for two drugs administered together for treatment of BRAF-positive anaplastic thyroid cancer**

problems, severe eye problems, fever that may be severe, serious skin reactions, high blood glucose levels or worsening diabetes, and serious anemia.

Severe adverse effects of trametinib include the development of new cancers; serious bleeding problems; inflammation of intestines and perforation of the intestines; blood clots in the arms, legs or lungs; heart problems; severe eye problems; lung or breathing problems; fever that may be severe; serious skin reactions; and high blood glucose levels or worsening diabetes.

Both drugs can cause harm to a developing fetus; women should be advised of the potential risk to the fetus and to use effective contraception.

**Source URL:**

<http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-new-uses-two-drugs-administered-together-treatment-braf-positive>

## [Supplemental Approvals](#)

### Generic Name (Trade Name—Company)

May 7, 2018

### **Tisagenlecleucel**

**(Kymriah—Novartis)**

**Agent receives second FDA approval to refractory or relapsed large B-cell lymphoma**

### Uses/Notes

FDA has approved [tisagenlecleucel suspension](#) for I.V. infusion for its second indication—treatment of adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. It is not indicated for treatment of patients with primary central nervous system lymphoma.

The agent was the first chimeric antigen receptor T cell (CAR-T) therapy to receive regulatory approval in August 2017 to treat patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

Tisagenlecleucel is now the only CAR-T cell therapy to receive FDA approval for two distinct indications in non-Hodgkin lymphoma (NHL) and B-cell ALL

### Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/agent-receives-second-fda-approval-refractory-or-relapsed-large-b-cell>

## Supplemental Approvals

### Generic Name (Trade Name—Company)

May 7, 2018

### **Tisagenlecleucel**

**(Kymriah—Novartis)**

**Agent receives second FDA approval for treatment of refractory or relapsed large B-cell lymphoma**

### Uses/Notes

FDA has approved [tisagenlecleucel suspension](#) for I.V. infusion for its second indication—treatment of adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. It is not indicated for treatment of patients with primary central nervous system lymphoma.

The agent was the first chimeric antigen receptor T cell (CAR-T) therapy to receive approval in August 2017 to treat patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

Tisagenlecleucel is now the only CAR-T cell therapy to receive FDA approval for two distinct indications in non-Hodgkin lymphoma (NHL) and B-cell ALL

### Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/agent-receives-second-fda-approval-treatment-refractory-or-relapsed-large-b>





## [New Drug Approvals](#)

### Generic Name (Trade Name—Company)

May 7, 2018

### **Coagulation factor Xa (recombinant), inactivated-zhzo**

**(*Andexxa—Portola*)**

### **FDA approves first and only antidote for reversal of Factor Xa inhibitors**

### Uses/Notes

FDA has [approved](#) coagulation factor Xa (recombinant), inactivated-zhzo, the first and only antidote indicated for patients treated with rivaroxaban and apixaban, when reversal of anticoagulation is needed because of life-threatening or uncontrolled bleeding.

The agent is a recombinant protein specifically designed to bind to Factor Xa inhibitors and rapidly reverse their anticoagulant effect. A modified form of the human Factor Xa molecule, it works by acting as a decoy for oral and injectable Factor Xa inhibitors, which target and bind to Factor Xa, which allows them to exert their anticoagulant effect. When the agent is given to a patient with Factor Xa inhibitor-related bleeding, it binds to the Factor Xa inhibitor and prevents it from inhibiting the activity of Factor Xa and reverses the anticoagulant effects of the inhibitor.

Approval was supported by data from two Phase III ANNEXA studies (ANNEXA-R and ANNEXA-A) that evaluated its safety and efficacy in reversing the anticoagulant activity of the Factor Xa inhibitors rivaroxaban and apixaban in healthy volunteers. Results demonstrated that the agent rapidly and significantly reversed anti-Factor Xa activity. The median decrease in anti-Factor Xa activity from baseline was 97% for rivaroxaban and 92% for apixaban.

### Source URL:

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-first-and-only-antidote-reversal-factor-xa-inhibitors>

## [Alerts and Recalls](#)

### Generic Name (Trade Name—Company)

May 14, 2018

### **Piperacillin and tazobactam for injection, 3.375 g vials**

***(No trade name—AuroMedics Pharma)***

**Recalled product contains glass particulate matter**

### Uses/Notes

AuroMedics Pharma is voluntarily [recalling](#) two lots (PP0317061-A, exp. Aug 2019, and PP0317049-A, exp. Aug 2019) of piperacillin and tazobactam for injection, 3.375 g (piperacillin sodium equivalent to 3 g of piperacillin and tazobactam sodium equivalent to 0.375 g of tazobactam) to the hospital level. Each single-dose vial contains 7.05 mEq (162 mg) of sodium.

The medication is packaged in a carton containing 10 single-dose vials (NDC: 55150-120-30).

The products have been found to contain particulate matter, visible only after reconstitution, that was confirmed to be glass within the vial.

Administration of a glass particulate, if present in I.V. drug, may result in local irritation or swelling in response to the foreign material. More serious potential outcomes would include blockage and clotting in blood vessels, which may be life-threatening.

Piperacillin and tazobactam for injection is used for treatment of patients with moderate to severe infections caused by susceptible isolates of the designated bacteria in intra-abdominal, skin and skin structure, and female pelvic infections, as well as community acquired and nosocomial pneumonia.

AuroMedics Pharma is notifying its distributors and customers by recall letters and is arranging for return and replacement of all recalled product.

To date, AuroMedics Pharma has not received reports of any adverse events or identifiable safety concerns attributed to use of the product from these lots.

### Source URL:

<http://www.aphadruginfoline.com/alerts-and-recalls/recalled-product-contains-glass-particulate-matter>

## Supplemental Approvals

### Generic Name (Trade Name—Company)

May 14, 2018

### Fingolimod

### Uses/Notes

FDA approved [fingolimod](#) to treat relapsing multiple sclerosis (MS) in children and adolescents aged 10 years and older. This is the first FDA approval of a drug to treat MS in pediatric patients.

Fingolimod was first approved by FDA in 2010 to treat adults with relapsing MS.

Approval was based on a clinical trial evaluating the effectiveness of fingolimod in treating 214 patients aged 10 to 17 with MS. The trial compared fingolimod with another MS drug, interferon beta-1a.

In the study, 86% of patients receiving fingolimod remained relapse-free after 24 months of treatment, compared with 46% of those receiving interferon beta-1a.

Adverse effects of fingolimod in pediatric trial participants were similar to those seen in adults. The most common adverse effects were headache, liver enzyme elevation, diarrhea, cough, flu, sinusitis, back pain, abdominal pain, and pain in extremities.

Fingolimod must be dispensed with a patient Medication Guide explaining serious risks, including slowing of the heart rate, especially after the first dose. Fingolimod may increase the risk of serious infections. Patients should be monitored for infection during treatment and for 2 months after treatment is discontinued.

Progressive multifocal leukoencephalopathy (PML), a rare brain infection that usually leads to death or severe disability, has been reported in patients being treated with fingolimod. PML cases usually occur in patients with weakened immune systems.

Fingolimod can cause vision problems and may increase the risk posterior reversible encephalopathy syndrome. Other serious risks include respiratory problems, liver injury, increased blood pressure, and skin cancer.

Fingolimod can cause harm to a developing fetus; women of child-bearing age should be advised of the

**(*Gilenya—Novartis*)**

**FDA approves first drug to treat MS in pediatric patients**

potential risk to the fetus and to use effective contraception.

**Source URL:**

<http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-first-drug-treat-ms-pediatric-patients>

## [Supplemental Approvals](#)

### Generic Name (Trade Name—Company)

May 14, 2018

**Polyethylene glycol 3350, sodium ascorbate, sodium sulfate, ascorbic acid, sodium chloride, and potassium chloride for oral solution**

***(Plenvu—Valeant/Salix)***

**Lower-volume bowel cleansing prep for colonoscopies receives FDA approval**

### Uses/Notes

[Salix Pharmaceuticals announced](#) FDA approval of polyethylene glycol 3350, sodium ascorbate, sodium sulfate, ascorbic acid, sodium chloride, and potassium chloride for oral solution, a lower-volume (1L) polyethylene glycol based (PEG) bowel preparation, under the trade name Plenvu.

Plenvu is the lowest, total-volume preparation bowel cleanser available in the United States, according to Salix.

Approval was based on multiple Phase III clinical trials, including the NOCT study, which compared Plenvu versus a trisulfate bowel cleansing solution (Suprep) using a two-day split-dosing regimen in adults. Both primary endpoints were met, achieving noninferior overall bowel cleansing success and “excellent plus good” cleansing of the ascending colon.

Plenvu is also the only FDA-approved bowel cleanser to offer split dosing on the same day as the colonoscopy procedure.

### Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/lower-volume-bowel-cleansing-prep-colonoscopies-receives-fda-approval>

## [Supplemental Approvals](#)

### Generic Name (Trade Name—Company)

May 15, 2018

### Epoetin alfa-epbx

*(Retacrit—Hospira)*

**FDA approves first epoetin alfa biosimilar for treatment of anemia**

### Uses/Notes

FDA approved [epoetin alfa-epbx](#) as a biosimilar to epoetin alfa (Epogen/Procrit) to treat anemia caused by chronic kidney disease, chemotherapy, or use of zidovudine in patients with HIV infection.

Epoetin alfa-epbx is also approved for use before and after surgery to reduce the chance that red blood cell transfusions will be needed because of blood loss during surgery.

Approval was based on a review of evidence that included extensive structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamic data, clinical immunogenicity data, and other clinical safety and effectiveness data that demonstrate the product is biosimilar to epoetin alfa. It has been approved as a [biosimilar](#), not as an [interchangeable product](#).

The most common adverse effects in clinical studies of the reference product were high blood pressure, joint pain, muscle spasm, fever, dizziness, medical device malfunction, blood vessel blockage, respiratory infection, cough, rash, injection site irritation, nausea, vomiting, muscle pain, inflammation of the mouth and lips, weight decrease, reduction in white blood cells, bone pain, high blood sugar, insomnia, headache, depression, difficulty swallowing, low blood potassium, blood clots, itching, headache, injection site pain, and chills.

Like epoetin alfa, the biosimilar must be dispensed with a patient Medication Guide and contains a boxed warning to alert health professionals and patients about increased risks of death, heart problems, stroke, and tumor growth or recurrence.

Additional warnings include high blood pressure; seizures; a condition in which the bone marrow stops making red blood cells, thus causing anemia; serious allergic reactions; and severe skin reactions.

### Source URL:

<http://www.aphadruginfoline.com/supplemental-approvals/fda-approves-first-epoetin-alfa-biosimilar-treatment-anemia>

## [New Drug Approvals](#)

### Generic Name (Trade Name—Company)

May 17, 2018

### Lucemyra

### Uses/Notes

FDA has approved [lofexidine hydrochloride](#), an oral, selective alpha 2-adrenergic receptor agonist that reduces the release of norepinephrine, to mitigate withdrawal symptoms from abrupt discontinuation of opioids in adults.

Norepinephrine is believed to play a role in many of the symptoms of opioid withdrawal. While the agent may lessen the severity of withdrawal symptoms, it may not completely prevent them and is only approved for treatment for up to 14 days.

It is not a treatment for opioid use disorder (OUD) but can be used as part of a broader, long-term treatment plan for managing OUD.

In patients using opioid analgesics appropriately as prescribed, opioid withdrawal is typically managed by slow taper of the medication, which is intended to avoid or lessen the effects of withdrawal while allowing the body to adapt to not having the opioid.

In patients with OUD, withdrawal is typically managed by substitution of another opioid, followed by gradual reduction or transition to maintenance therapy with FDA-approved medication-assisted treatment drugs such as methadone, buprenorphine or naltrexone; or by various medications aimed at specific symptoms, such as OTC remedies for upset stomach or aches and pains. Other treatments may also be prescribed.

Safety and efficacy of lofexidine were supported by two randomized, double-blind, placebo-controlled clinical trials of 866 adults meeting Diagnostic and Statistical Manual–IV criteria for opioid dependence who were physically dependent on opioids and undergoing abrupt opioid discontinuation.

The studies evaluated benefit using the Short Opiate Withdrawal Scale of Gossop (SOWS-Gossop), a patient-reported outcome instrument that assesses opioid withdrawal symptoms such as stomach cramps, muscle spasms/twitching, feeling of coldness, heart pounding, muscular tension, aches and pains, yawning,



**(Lofexidine hydrochloride—US WorldMeds)**

**FDA approves first nonopioid to mitigate opioid withdrawal symptoms**

runny eyes, and insomnia or problems sleeping.

For each opioid withdrawal symptom, patients are asked to rate their symptom severity using four response options (none, mild, moderate, and severe), with the SOWS-Gossop total score ranging from 0 to 30. A higher score indicated a greater withdrawal symptom severity. SOWS-Gossop scores were lower for patients treated with lofexidine compared with placebo, and more patients completed the treatment period of the studies in the lofexidine group compared with the placebo group.

The most common adverse effects included hypotension, bradycardia, somnolence, sedation, and dizziness. Lofexidine was also associated with a few cases of fainting. It also affects the heart's electrical activity, which can increase the risk of abnormal heart rhythms. When the agent is stopped, patients can experience a marked increase in blood pressure.

Safety and efficacy have not been established in children or adolescents younger than 17 years of age. After a period of not using opioid drugs, patients may be more sensitive to the effects of lower amounts of opioids if relapse does occur, and taking opioids in amounts that were used before withdrawing from opioids can lead to overdose and death.

FDA is requiring 15 postmarketing studies, including both animal and human studies.

**Source URL:**

<http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-first-nonopioid-mitigate-opioid-withdrawal-symptoms>

## [New Drug Approvals](#)

### Generic Name (Trade Name—Company)

May 18, 2018

### Erenumab-aooe

*(Aimovig—Amgen)*

**Novel once-monthly drug prevents migraines in adults**

### Uses/Notes

FDA has approved [erenumab-aooe](#) for once-monthly preventive treatment of migraine in adults.

Given by self-injection, it is the first FDA-approved preventive migraine treatment in a new class of drugs that work by blocking the activity of calcitonin gene-related peptide, a molecule involved in migraine attacks.

“Aimovig provides patients with a novel option for reducing the number of days with migraine,” said an FDA spokesperson.

Effectiveness of the agent to prevent migraine was evaluated in three clinical trials. The first study, which included 955 participants with a history of episodic migraine, compared erenumab-aooe with placebo. Over a 6-month period, patients treated with erenumab-aooe experienced, on average, one to two fewer monthly migraine days than those on placebo.

The second study included 577 patients with a history of episodic migraine and compared erenumab-aooe with placebo. Over 3 months, patients experienced, on average, one fewer migraine day per month than those on placebo.

In the third study of 667 patients with a history of chronic migraine, patients treated with erenumab-aooe over the course of 3 months experienced, on average, 2.5 fewer monthly migraine days than those receiving placebo.

The most common adverse effects were injection-site reactions and constipation.

### Source URL:

<http://www.aphadruginfo.com/new-drug-approvals/novel-once-monthly-drug-prevents-migraines-adults>

APhA DrugInfoLine is an official publication of, and is owned and copyrighted by the American Pharmacists Association, the national professional society of pharmacists. Materials in APhA DrugInfoLine do not necessarily represent the policy, recommendations, or endorsement of APhA. The publisher, authors, editors, reviewers, and contributors have taken care to ensure that information contained in APhA DrugInfoLine is accurate and current; however, they shall have no liability to any person or entity with regard to claims, losses, or damages caused or alleged to be caused, directly or indirectly, by use of any information contained in the publication. All decisions about drug therapy must be based on the independent judgment of the clinician. Copyright © 2000–2011, American Pharmacists Association. All rights reserved.