



FDA Drug Safety Communication

FDA reinforces safety information about serious low blood sugar levels and mental health side effects with fluoroquinolone antibiotics; requires label changes

Safety Announcement

[07-10-2018] The Food and Drug Administration (FDA) is strengthening the current warnings in the prescribing information that fluoroquinolone antibiotics may cause significant decreases in blood sugar and certain mental health side effects. The low blood sugar levels can result in serious problems, including coma, particularly in older people and patients with diabetes who are taking medicines to reduce blood sugar. We are making these changes because our recent review found reports of life-threatening low blood sugar side effects and reports of additional mental health side effects.

We are 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 sugar disturbances, including high blood sugar and low blood sugar, are already included as a warning in most fluoroquinolone drug labels; however, we are adding that low blood sugar levels, also called hypoglycemia, can lead to coma.

Across the fluoroquinolone antibiotic class, a range of mental health side 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 side effects more prominent and more consistent across the systemic fluoroquinolone drug class. The mental health side 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 called delirium.

Fluoroquinolone antibiotics are approved to treat certain serious bacterial infections, and have been used for more than 30 years. They work by killing or stopping the growth of bacteria that can cause illness. Without treatment, some infections can spread and lead to serious health problems (see List of Currently Available FDA-Approved [Fluoroquinolones](#) for Systemic Use).

Patients should tell your health care professionals if you are taking a diabetes medicine when your health care professional is considering prescribing an antibiotic, and also if you have low blood sugar or symptoms of it while taking a fluoroquinolone. For patients with diabetes, your health care professional may ask you to check your blood sugar more often while taking a fluoroquinolone. Early signs and symptoms of low blood sugar include:

- Confusion
- Pounding heart or very fast pulse

- Dizziness
- Feeling shaky
- Unusual hunger
- Headaches
- Irritability
- Pale skin
- Sweating
- Trembling
- Weakness
- Unusual anxiety

Discuss with your health care professional how to treat yourself if you suspect low blood sugar. Symptoms of low blood sugar can progress and become life-threatening, so seek help immediately by calling 911 or going to an emergency room if you experience more serious symptoms, including confusion, inability to complete routine tasks, blurred vision, seizures, or loss of consciousness. Patients should also tell your health care professional immediately if you notice any changes in your mood, behavior, or thinking. Read the patient Medication Guide you receive with your fluoroquinolone antibiotic prescription, which explains the benefits and risks of the medicine.

Health care professionals should be aware of the potential risk of hypoglycemia sometimes resulting in coma, occurring more frequently in the elderly and those with diabetes taking an oral hypoglycemic medicine or insulin. Alert patients of the symptoms of hypoglycemia and 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 side effects, including psychiatric adverse reactions, or blood glucose disturbances and switch to a non-fluoroquinolone antibiotic if possible. Stop fluoroquinolone treatment immediately if a patient reports serious side effects involving the tendons, muscles, joints, or nerves, and switch to a non-fluoroquinolone antibiotic to complete the patient’s treatment course. Health care 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.

FDA continues to monitor and evaluate the safety and effectiveness of medicines after we approve them and they go on the market. In the case of fluoroquinolones, we reviewed reports of cases submitted to FDA* and the published medical literature of apparently healthy patients who experienced serious changes in mood, behavior, and blood sugar levels while being treated with systemic fluoroquinolones (see Data Summary for information on the names of fluoroquinolones and numbers of reports). Some of the mental health side effects are already listed in some of the labels and some events are listed using similar terms, but not all fluoroquinolone labels provided this information. As a result, we are requiring several changes to the *Warnings and Precautions* section in the fluoroquinolones drug labels. Details will be added describing hypoglycemic coma, and the new subheading “Psychiatric Adverse Reactions” found under “Central Nervous System Effects” will help clarify and identify the mental health side effects.

We previously communicated about other safety issues associated with fluoroquinolones in [May 2016](#) (restricting use for certain uncomplicated infections), [July 2016](#) (disabling side effects), [August 2013](#) (peripheral neuropathy), and [July 2008](#) (tendinitis and tendon rupture).

We urge patients and health care professionals to report side effects involving fluoroquinolones or other drugs to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

*The cases were reported to the [FDA Adverse Event Reporting System \(FAERS\)](#).

List of FDA-Approved Fluoroquinolones for Systemic Use

Brand Name	Active Ingredient
Avelox	moxifloxacin ⁺
Baxdela	delafloxacin
Cipro	ciprofloxacin ⁺
Cipro extended-release [±]	ciprofloxacin extended-release
Factive	gemifloxacin ⁺
Levaquin	levofloxacin ⁺
Ofloxacin (Generic brand) [±]	ofloxacin

⁺ available as brand and generic

[±] available only as generic

Facts about Fluoroquinolones

- Fluoroquinolones are a class of antibacterial medicines approved to treat certain kinds of infections caused by bacteria.
- Fluoroquinolones should not be prescribed for patients who have other treatment options for [acute bacterial sinusitis \(ABS\)](#), [acute bacterial exacerbation of chronic bronchitis \(ABECB\)](#), and [uncomplicated urinary tract infections \(UTI\)](#) because the risks outweigh the benefits in these patients and other antibiotics to treat these conditions are available.
- There are several brand and generic names (see List of DA-Approved Fluoroquinolones for Systemic Use).
- Fluoroquinolones work by killing or stopping the growth of bacteria that can cause illness. Like other antibacterial medicines, fluoroquinolones do not treat infections caused by viruses such as colds or the flu.
- Common side effects include nausea, diarrhea, headache, dizziness, lightheadedness, or trouble sleeping.
- Symptoms of serious side effects include unusual joint or tendon pain, muscle weakness, a “pins and needles” tingling or pricking sensation, numbness in the arms or legs, confusion, hallucinations, and significantly low blood sugar levels.

Data Summary

FDA conducted a review of postmarketing adverse event data on hypoglycemic coma for all five fluoroquinolones approved at the time FDA completed its safety analysis. These were ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, and ofloxacin. A new fluoroquinolone, delafloxacin, was approved on June 19, 2017, and was not included in the class review.

However, FDA anticipates the same adverse reactions are likely for delafloxacin because the drug is within the class of fluoroquinolones. Thus, the safety label changes will also apply to delafloxacin. The safety review was based on postmarketing adverse event reports found in the [FDA Adverse Event Reporting System](#) (FAERS) database and published medical literature.

Hypoglycemic Coma

Hypoglycemic coma, which our review found has resulted in death in some cases, is not listed in any of the current fluoroquinolone drug labels. However, hypoglycemia associated with fluoroquinolone use is listed in five of the drug labels, and one (moxifloxacin) describes the occurrence of dysglycemia predominantly in elderly diabetic patients receiving concomitant treatment with an oral hypoglycemic agent or with insulin. Four of the fluoroquinolones have a labeled drug interaction with sulfonylurea agents, which can cause hypoglycemia.

In our search of hypoglycemic coma associated with fluoroquinolones, we identified 56 reports in a FAERS search from October 1987 through April 2017, and 11 additional cases in the medical literature. Most patients had risk factors for hypoglycemia such as older age, diabetes, renal insufficiency, and concomitant use of hypoglycemic drugs, especially sulfonylureas.

Patients were being treated with levofloxacin (n=44), ciprofloxacin (n=12), moxifloxacin (n=9), and ofloxacin (n=2). Of the 47 patients documented to be diabetic, 41 were reportedly taking one or more of 19 different oral hypoglycemic drugs or combinations of drugs. Three patients reported using insulin only, one patient was treated with diet alone, and diabetic drugs were not documented in two patients. Thirty-five of the 47 were taking a sulfonylurea drug. Twenty of the 67 patients who experienced hypoglycemic coma did not have diabetes and were not reported to be taking oral hypoglycemic agents or insulin.

Thirteen deaths occurred. Some of these patients were being treated with fluoroquinolones for relatively uncomplicated infections such as urinary tract or upper respiratory tract infections, and for post-operative prophylaxis. Others had documented renal insufficiency, which increases a patient's risk for hypoglycemia and is an independent risk factor for death.

After experiencing hypoglycemic coma, nine of the 54 patients who lived did not recover fully and had resultant disability. Four of the nine patients remained comatose for at least a month after their blood glucose levels normalized. Five of the nine patients were described as having experienced varying degrees of neurological injury.

Psychiatric Adverse Reactions

Across the fluoroquinolone antibiotic class, a range of psychiatric adverse reactions are already described in the *Warnings and Precautions* section under *Central Nervous System Effects*, which differed by individual drug. FDA conducted a class review of postmarketing adverse event data on select psychiatric adverse events associated with the five FDA-approved fluoroquinolones, which at that time did not include delafloxacin. The safety review was based on an analysis of postmarketing adverse event reports contained in the FAERS database and published medical literature. We found that psychiatric adverse reactions were not consistent in the drug labels.

The labels of fluoroquinolones currently include many psychiatric adverse reactions in the *Warnings and Precautions* section, for example, hallucination, psychoses, confusion, depression, anxiety, and paranoia. In an effort to harmonize the psychiatric adverse reactions described in the drug labels across the class of fluoroquinolones, we are requiring that all fluoroquinolones include six psychiatric adverse reactions (disturbance in attention, memory impairment, delirium, nervousness, agitation, and disorientation) in the *Central Nervous System Effects* of the *Warnings and Precautions* section of the labels. Disturbance in attention, memory impairment, and delirium are new adverse reactions to be added to the labels of the entire class of fluoroquinolones. Nervousness, agitation, and disorientation had been previously listed in the fluoroquinolone drug labels and will now be added to the *Warnings and Precautions* section of each drug label to harmonize labels across the fluoroquinolone drug class. The new label changes will make the psychiatric adverse reactions more prominent and more consistent.

Related Information

- [The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective](#)
- [FDA approves safety labeling changes for fluoroquinolones](#)
- [Think It Through: Managing the Benefits and Risks of Medicines](#)