

17.5 Plague and Anthrax Studies

Patients given LEVAQUIN[®] for these conditions should be informed that efficacy studies could not be conducted in humans for ethical and feasibility reasons. Therefore, approval for these conditions was based on efficacy studies conducted in animals.

Active Ingredient Made in Japan

Finished Product Manufactured by:

- Janssen Ortho LLC, Gurabo, Puerto Rico 00778 (for the Tablets).
- Janssen Pharmaceutica N.V., Beerse, Belgium (for the Oral Solution and Injection, Single-Use Vials).
- Hospira, Inc., Austin, TX 78728 (for the Injection Pre-Mixed Solution Single-Use in Flexible Container).

Manufactured for:

- Janssen Pharmaceuticals, Inc., Titusville, NJ 08560.

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17.6 FDA-Approved Medication Guide

MEDICATION GUIDE
LEVAQUIN[®] [Leave ah kwin]
(levofloxacin)
Tablets

LEVAQUIN[®] (levofloxacin)
Oral Solution

LEVAQUIN[®] (levofloxacin) Injection
for Intravenous Use

LEVAQUIN[®] (levofloxacin in 5% dextrose) Injection
for Intravenous Use

Read this Medication Guide before you start taking LEVAQUIN and each time you get a refill. There may be new information. This Medication Guide does not take

the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about LEVAQUIN? LEVAQUIN, a fluoroquinolone antibiotic, can cause serious side effects. Some of these serious side effects could result in death.

If you have any of the following serious side effects while you take LEVAQUIN, get medical help right away. Talk with your healthcare provider about whether you should continue to take LEVAQUIN.

1. Tendon rupture or swelling of the tendon (tendinitis).

- **Tendon problems can happen in people of all ages who take LEVAQUIN.** Tendons are tough cords of tissue that connect muscles to bones.

Some tendon problems include pain, swelling, tears, and inflammation of tendons including the back of the ankle (Achilles), shoulder, hand, or other tendon sites.

- The risk of getting tendon problems while you take LEVAQUIN is higher if you:
 - o are over 60 years of age
 - o are taking steroids (corticosteroids)
 - o have had a kidney, heart or lung transplant.
- Tendon problems can happen in people who do not have the above risk factors when they take LEVAQUIN.
- Other reasons that can increase your risk of tendon problems can include:
 - o physical activity or exercise
 - o kidney failure
 - o tendon problems in the past, such as in people with rheumatoid arthritis (RA)

- Call your healthcare provider right away at the first sign of tendon pain, swelling or inflammation. Stop taking LEVAQUIN until tendinitis or tendon rupture has been ruled out by your healthcare provider. Avoid exercise and using the affected area.

The most common area of pain and swelling is the Achilles tendon at the back of your ankle. This can also happen with other tendons. Talk to your healthcare provider about the risk of tendon rupture with continued use of LEVAQUIN. You may need a different antibiotic that is not a fluoroquinolone to treat your infection.

- Tendon rupture can happen while you are taking or after you have finished taking LEVAQUIN. Tendon ruptures have happened up to several months after people have finished taking their fluoroquinolone.
- Get medical help right away if you get any of the following signs or symptoms of a tendon rupture:
 - o hear or feel a snap or pop in a tendon area
 - o bruising right after an injury in a tendon area
 - o unable to move the affected area or bear weight

2. **Worsening of myasthenia gravis (a problem that causes muscle weakness).** Fluoroquinolones like LEVAQUIN may cause worsening of myasthenia gravis symptoms, including muscle weakness and breathing problems. Call your healthcare provider right away if you have any worsening muscle weakness or breathing problems.

- See “**What are the possible side effects of LEVAQUIN?**”

What is LEVAQUIN?

LEVAQUIN is a fluoroquinolone antibiotic medicine used in adults age 18 years or older to treat certain infections caused by certain germs called bacteria. These bacterial infections include:

- nosocomial pneumonia
- community-acquired pneumonia

- acute sinus infection
- acute worsening of chronic bronchitis
- skin infections, complicated and uncomplicated
- chronic prostate infection
- urinary tract infections, complicated and uncomplicated
- acute kidney infection (pyelonephritis)
- inhalational anthrax
- plague

Studies of LEVAQUIN for use in the treatment of plague and anthrax were done in animals only, because plague and anthrax could not be studied in people.

LEVAQUIN is also used to treat children who are 6 months of age or older and may have breathed in anthrax germs, have plague, or been exposed to plague germs.

It is not known if LEVAQUIN is safe and effective in children under 6 months of age.

The safety and effectiveness in children treated with LEVAQUIN for more than 14 days is not known.

Who should not take LEVAQUIN?

Do not take LEVAQUIN if you have ever had a severe allergic reaction to an antibiotic known as a fluoroquinolone, or if you are allergic to levofloxacin or any of the ingredients in LEVAQUIN. See the end of this leaflet for a complete list of ingredients in LEVAQUIN.

What should I tell my healthcare provider before taking LEVAQUIN?

Before you take LEVAQUIN, tell your healthcare provider if you:

- have tendon problems
- have a problem that causes muscle weakness (myasthenia gravis)
- have central nervous system problems such as seizures (epilepsy)

- have nerve problems
- have or anyone in your family has an irregular heartbeat, especially a condition called “QT prolongation”
- have low blood potassium (hypokalemia)
- have bone problems
- have joint problems including rheumatoid arthritis (RA)
- have kidney problems. You may need a lower dose of LEVAQUIN if your kidneys do not work well.
- have liver problems
- have diabetes or problems with low blood sugar (hypoglycemia)
- are pregnant or plan to become pregnant. It is not known if LEVAQUIN will harm your unborn child.
- are breastfeeding or plan to breastfeed. It is not known if LEVAQUIN passes into your breast milk. You and your healthcare provider should decide if you will take LEVAQUIN or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

LEVAQUIN and other medicines can affect each other causing side effects.

Especially tell your healthcare provider if you take:

- a steroid medicine.
- an anti-psychotic medicine
- a tricyclic antidepressant
- a water pill (diuretic)
- certain medicines may keep LEVAQUIN from working correctly. Take LEVAQUIN Tablets or Oral Solution either 2 hours before or 2 hours after taking these medicines or supplements:

- o an antacid, multivitamin, or other medicines or supplements that have magnesium, aluminum, iron, or zinc
- o sucralfate (Carafate[®])
- o didanosine (Videx[®], Videx[®] EC)
- a blood thinner (warfarin, Coumadin, Jantoven)
- an oral anti-diabetes medicine or insulin
- an NSAID (Non-Steroidal Anti-Inflammatory Drug). Many common medicines for pain relief are NSAIDs. Taking an NSAID while you take LEVAQUIN or other fluoroquinolones may increase your risk of central nervous system effects and seizures.
- theophylline (Theo-24[®], Elixophyllin[®], Theochron[®], Uniphyll[®], Theolair[®])
- a medicine to control your heart rate or rhythm (antiarrhythmics)

Ask your healthcare provider if you are not sure if any of your medicines are listed above.

Know the medicines you take. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take LEVAQUIN?

- Take LEVAQUIN exactly as your healthcare provider tells you to take it.
- Take LEVAQUIN at about the same time each day.
- Drink plenty of fluids while you take LEVAQUIN.
- LEVAQUIN Tablets can be taken with or without food.
- Take LEVAQUIN Oral Solution 1 hour before or 2 hours after eating.
- If you miss a dose of LEVAQUIN, take it as soon as you remember. Do not take more than 1 dose in 1 day.
- LEVAQUIN for Injection is given by slow intravenous (I.V.) infusion into your vein over 60 or 90 minutes as prescribed by your healthcare provider.

- Do not skip any doses of LEVAQUIN or stop taking it, even if you begin to feel better, until you finish your prescribed treatment unless:
 - o you have tendon problems. See **“What is the most important information I should know about LEVAQUIN?”**.
 - o you have a serious allergic reaction. See **“What are the possible side effects of LEVAQUIN?”**.
 - o your healthcare provider tells you to stop taking LEVAQUIN

Taking all of your LEVAQUIN doses will help make sure that all of the bacteria are killed. Taking all of your LEVAQUIN doses will help you lower the chance that the bacteria will become resistant to LEVAQUIN. If your infection does not get better while you take LEVAQUIN, it may mean that the bacteria causing your infection may be resistant to LEVAQUIN. If your infection does not get better, call your healthcare provider. If your infection does not get better, LEVAQUIN and other similar antibiotic medicines may not work for you in the future.

- If you take too much LEVAQUIN, call your healthcare provider or get medical help right away.

What should I avoid while taking LEVAQUIN?

- LEVAQUIN can make you feel dizzy and lightheaded. Do not drive, operate machinery, or do other activities that require mental alertness or coordination until you know how LEVAQUIN affects you.
- Avoid sunlamps, tanning beds, and try to limit your time in the sun. LEVAQUIN can make your skin sensitive to the sun (photosensitivity) and the light from sunlamps and tanning beds. You could get severe sunburn, blisters or swelling of your skin. If you get any of these symptoms while you take LEVAQUIN, call your healthcare provider right away. You should use a sunscreen and wear a hat and clothes that cover your skin if you have to be in sunlight.

What are the possible side effects of LEVAQUIN?

LEVAQUIN can cause serious side effects, including:

- See **“What is the most important information I should know about LEVAQUIN?”**

- **Serious allergic reactions.**

Allergic reactions can happen in people taking fluoroquinolones, including LEVAQUIN, even after only 1 dose. Stop taking LEVAQUIN and get emergency medical help right away if you have any of the following symptoms of a severe allergic reaction:

- o hives
- o trouble breathing or swallowing
- o swelling of the lips, tongue, face
- o throat tightness, hoarseness
- o rapid heartbeat
- o faint
- o skin rash

Skin rash may happen in people taking LEVAQUIN, even after only 1 dose. Stop taking LEVAQUIN at the first sign of a skin rash and call your healthcare provider. Skin rash may be a sign of a more serious reaction to LEVAQUIN.

- **Liver damage (hepatotoxicity):** Hepatotoxicity can happen in people who take LEVAQUIN. Call your healthcare provider right away if you have unexplained symptoms such as:

- o nausea or vomiting
- o stomach pain
- o fever
- o weakness
- o abdominal pain or tenderness
- o itching
- o unusual tiredness
- o loss of appetite

- o light colored bowel movements
- o dark colored urine
- o yellowing of your skin or the whites of your eyes

Stop taking LEVAQUIN and tell your healthcare provider right away if you have yellowing of your skin or white part of your eyes, or if you have dark urine. These can be signs of a serious reaction to LEVAQUIN (a liver problem).

- **Central Nervous System Effects.** Seizures have been reported in people who take fluoroquinolone antibiotics including LEVAQUIN. Tell your healthcare provider if you have a history of seizures. Ask your healthcare provider whether taking LEVAQUIN will change your risk of having a seizure.

Central Nervous System (CNS) side effects may happen as soon as after taking the first dose of LEVAQUIN. Talk to your healthcare provider right away if you get any of these side effects, or other changes in mood or behavior:

- o seizures
- o hear voices, see things, or sense things that are not there (hallucinations)
- o feel restless
- o tremors
- o feel anxious or nervous
- o confusion
- o depression
- o trouble sleeping
- o nightmares
- o feel lightheaded
- o feel more suspicious (paranoia)

- o suicidal thoughts or acts
- o a headache that will not go away, with or without blurred vision.

- **Intestine infection (Pseudomembranous colitis)**

Pseudomembranous colitis can happen with many antibiotics, including LEVAQUIN. Call your healthcare provider right away if you get watery diarrhea, diarrhea that does not go away, or bloody stools. You may have stomach cramps and a fever. Pseudomembranous colitis can happen 2 or more months after you have finished your antibiotic.

- **Changes in sensation and nerve damage (Peripheral Neuropathy)**

Damage to the nerves in arms, hands, legs, or feet can happen in people taking fluoroquinolones, including LEVAQUIN. Stop LEVAQUIN and talk with your healthcare provider right away if you get any of the following symptoms of peripheral neuropathy in your arms, hands, legs, or feet:

- o pain
- o burning
- o tingling
- o numbness
- o weakness

The nerve damage may be permanent.

- **Serious heart rhythm changes (QT prolongation and torsades de pointes)**

Tell your healthcare provider right away if you have a change in your heart beat (a fast or irregular heartbeat), or if you faint. LEVAQUIN may cause a rare heart problem known as prolongation of the QT interval. This condition can cause an abnormal heartbeat and can be very dangerous. The chances of this happening are higher in people:

- o who are elderly
- o with a family history of prolonged QT interval
- o with low blood potassium (hypokalemia)

- o who take certain medicines to control heart rhythm (antiarrhythmics)

- **Joint Problems**

Increased chance of problems with joints and tissues around joints in children can happen. Tell your child's healthcare provider if your child has any joint problems during or after treatment with LEVAQUIN.

- **Changes in blood sugar**

People who take LEVAQUIN and other fluoroquinolone medicines with oral anti-diabetes medicines or with insulin can get low blood sugar (hypoglycemia) and high blood sugar (hyperglycemia). Follow your healthcare provider's instructions for how often to check your blood sugar. If you have diabetes and you get low blood sugar while taking LEVAQUIN, stop taking LEVAQUIN and call your healthcare provider right away. Your antibiotic medicine may need to be changed.

- **Sensitivity to sunlight (photosensitivity)**

See "**What should I avoid while taking LEVAQUIN?**"

The most common side effects of LEVAQUIN include:

- o nausea
- o headache
- o diarrhea
- o insomnia
- o constipation
- o dizziness

In children 6 months and older who take LEVAQUIN to treat anthrax disease or plague, vomiting is also common.

Low blood pressure can happen when LEVAQUIN is given too fast by IV injection. Tell your healthcare provider if you feel dizzy or faint during a treatment with LEVAQUIN Injection.

LEVAQUIN may cause false-positive urine screening results for opiates when testing is done with some commercially available kits. A positive result should be confirmed using a more specific test.

These are not all the possible side effects of LEVAQUIN. Tell your healthcare provider about any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store LEVAQUIN?

- Store LEVAQUIN Tablets at 59°F to 86° F (15°C to 30°C).
- Keep LEVAQUIN Tablets in a tightly closed container.
- Store LEVAQUIN Oral Solution at 59°F to 86° F (15°C to 30°C).

Keep LEVAQUIN and all medicines out of the reach of children.

General information about the safe and effective use of LEVAQUIN

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use LEVAQUIN for a condition for which it is not prescribed. Do not give LEVAQUIN to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about LEVAQUIN. If you would like more information about LEVAQUIN, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about LEVAQUIN that is written for healthcare professionals.

For more information go to www.levaquin.com or call 1-800-526-7736.

What are the ingredients in LEVAQUIN?

LEVAQUIN Tablets, LEVAQUIN Oral Solution, LEVAQUIN Injection in Single-Use Vials and LEVAQUIN Injection Premix in Single-Use Flexible Containers:

Active ingredient: levofloxacin

All LEVAQUIN Tablets:

Inactive ingredients: crospovidone, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, titanium dioxide.

LEVAQUIN 250 mg Tablets also contain synthetic red iron oxide.

LEVAQUIN 500 mg Tablets also contain synthetic red iron oxide and synthetic yellow iron oxide.

LEVAQUIN Oral Solution:

Inactive ingredients: artificial and natural flavors, ascorbic acid, benzyl alcohol, caramel color, glycerin, hydrochloric acid, propylene glycol, purified water, sucralose, and sucrose. It may also contain a solution of sodium hydroxide for pH adjustment.

LEVAQUIN Injection in Single-Use Vials:

Inactive ingredients: water for injection. LEVAQUIN for Injection Single Use Vials do not contain any preservatives.

LEVAQUIN Injection Premix in Single-Use Flexible Containers:

Inactive ingredients: Dextrose (D5W). Solutions of hydrochloric acid and sodium hydroxide may have been added to adjust the pH.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Active Ingredient Made in Japan

Finished Product Manufactured by:

Janssen Ortho LLC, Gurabo, Puerto Rico 00778 (Tablets).

Janssen Pharmaceutica N.V., Beerse, Belgium (Oral Solution, Injection Single-Use Vials).

Hospira, Inc., Austin, TX 78728 (Injection Premix).

Manufactured for:

Janssen Pharmaceuticals, Inc., Titusville, NJ 08560.

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