HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LEVAQUIN® safely and effectively. See full prescribing information for LEVAQUIN.

LEVAQUIN® (levofloxacin) Tablet, Film Coated for Oral use
LEVAQUIN® (levofloxacin) Solution for Oral use
LEVAQUIN® (levofloxacin) Injection, Solution, Concentrate for Intravenous use
LEVAQUIN® (levofloxacin) Injection, Solution, for Intravenous use

Initial U.S. Approval: 1996

WARNING:
Fluoroquinolones, including LEVAQUIN®, are associated with an increased risk of tendinopathy and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants (See Warnings and Precautions (5.1)).

To reduce the development of drug-resistant bacteria and maintain the effectiveness of LEVAQUIN® and other antibacterial drugs, LEVAQUIN® should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

RECENT MAJOR CHANGES
- Tendinopathy and Tendon Rupture (5.1) 9/2008

INDICATIONS AND USAGE
- Tendinopathy and Tendon Rupture (including rupture), especially with concomitant corticosteroid use

Recent U.S. Approval: 2009

CONTRAINDICATIONS
- Known hypersensitivity to LEVAQUIN® or other fluoroquinolones

WARNINGS AND PRECAUTIONS
- Risk of tendinopathy and tendon rupture is increased. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants. Discontinue if pain or inflammation in a tendon occurs (5.1, 8.5)
- Anaphylactic reactions and allergic skin reactions, serious, occasionally fatal, may occur after first dose (4, 5.2)
- Hematologic (including agranulocytosis, thrombocytopenia), and renal toxicities may occur after multiple doses (8.3)
- Hepatotoxicity: Severe, and sometimes fatal, hepatoxicity has been reported. Discontinue immediately if signs and symptoms of hepatitis occur (5.4)
- Central nervous system effects, including convulsions, anxiety, confusion, depression, and insomnia may occur after the first dose. Use with caution in patients with known or suspected disorders that may predispose them to seizures or lower the seizure threshold (5.5)
- Clostridium difficile-associated colitis: evaluate if diarrhea occurs (5.6)
- Peripheral neuropathy: discontinue if symptoms occur in order to prevent irreversibility (5.7)
- Prolongation of the QT interval and isolated cases of torsade de pointes have been reported. Avoid use in patients with known prolongation, those with hypokalemia, and with other drugs that prolong the QT interval (5.8, 8.5)

ADVERSE REACTIONS
- The most common reactions (≥ 3%) were nausea, headache, diarrhea, insomnia, constipation and dizziness (6.2)

To report SUSPECTED ADVERSE REACTIONS, contact Ortho-McNeil-Janssen Scientific Affairs Customer Communications Center at 1-800-526-7736 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS
- Multivalent cation-containing products including antacids, metal cations or didanosine
- Absorption of levofloxacin is decreased when the tablet or oral solution formulation is taken within 2 hours of these products. Do not co-administer the intravenous formulation in the same IV line with a multivalent cation, e.g., magnesium (2.4, 7.1)
- Warfarin
- Effect may be enhanced. Monitor prothrombin time, INR, watch for bleeding (7.2)
- Antidiabetic agents
- Carefully monitor blood glucose (5.10, 7.3)

USE IN SPECIFIC POPULATIONS
- Geriatrics: Severe hepatotoxicity has been reported. The majority of reports describe patients 65 years of age or older (8.4, 8.5, 17). May have increased risk of tendinopathy (including rupture), especially with concomitant corticosteroid use (5.1, 8.5, 17). May be more susceptible to prolongation of the QT interval (5.8, 8.5, 17)
- Pediatrics: Musculoskeletal disorders (arthritis, arthralgia, tendinopathy, and gait abnormality) seen in more LEVAQUIN®-treated patients than in comparator. Shown to cause arthropathy and osteochondrosis in juvenile animals (5.9, 8.4, 13.2). Safety in pediatric patients treated for more than 14 days has not been studied. Risk-benefit appropriate only for the treatment of inhalational anthrax (post-exposure) (1.13, 2.2, 8.4, 14.9)

See 17 for PATIENT COUNSELING INFORMATION and the FDA-approved Medication Guide

Revised: 07/2009
LEVAQUIN® (levofloxacin)

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1 INDICATIONS AND USAGE
To reduce the development of drug-resistant bacteria and maintain the effectiveness of LEVAQUIN® and other antibacterial drugs, LEVAQUIN® should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

LEVAQUIN® Tablets/Injection and Oral Solution are indicated for the treatment of adults (≥ 18 years of age) with mild, moderate, and severe infections caused by susceptible strains of the designated microorganisms in the conditions listed in this section. LEVAQUIN® Injection is indicated when intravenous administration offers a route of administration advantageous to the patient (e.g., patient cannot tolerate an oral dosage form).

Culture and susceptibility testing
Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing the infection and to determine their susceptibility to levofloxacin [See Clinical Pharmacology (12.4)]. Therapy with LEVAQUIN® may be initiated before results of these tests are known; once results become available, appropriate therapy should be selected.

As with other drugs in this class, some strains of Pseudomonas aeruginosa may develop resistance fairly rapidly during treatment with LEVAQUIN®. Culture and susceptibility testing performed periodically during therapy will provide information about the continued susceptibility of the pathogens to the antimicrobial agent and also the possible emergence of bacterial resistance.

1.1 Nosocomial Pneumonia
LEVAQUIN® is indicated for the treatment of nosocomial pneumonia due to methicillin-susceptible Staphylococcus aureus, Pseudomonas aeruginosa, Serratia marcescens, Escherichia coli, Klebsiella pneumoniae, Haemophilus influenzae, or Strepptococcus pneumoniae. Adjunctive therapy should be used as clinically indicated. Where Pseudomonas aeruginosa is a documented or presumptive pathogen, combination therapy with an anti-pseudomonal ß-lactam is recommended (see Clinical Studies (14.1)).

1.2 Community-Acquired Pneumonia: 7-14 day Treatment Regimen
LEVAQUIN® is indicated for the treatment of community-acquired pneumonia due to methicillin-susceptible Staphylococcus aureus, Streptococcus pneumoniae (including multi-drug-resistant Streptococcus pneumoniae [MDRSP]), Haemophilus influenzae, Haemophilus paraphlinuenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Chlamydia pneumoniae, Legionella pneumophila, or Mycoplasma pneumoniae (See Dosage and Administration (2.1) and Clinical Studies (14.2)).

MDRSP isolates are strains resistant to two or more of the following antibacterials: penicillin (MIC ≥ 2 mcg/mL), 2nd generation cephalosporins, e.g., cefuroxime, macrolides, tetracyclines and trimethoprim/sulfamethoxazole.

1.3 Community-Acquired Pneumonia: 5-day Treatment Regimen
LEVAQUIN® is indicated for the treatment of community-acquired pneumonia due to Streptococcus pneumoniae (excluding multi-drug-resistant strains [MDRSP]), Haemophilus influenzae, Haemophilus paraphlinuenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Chlamydia pneumoniae, Legionella pneumophila, or Mycoplasma pneumoniae [see Dosage and Administration (2.1) and Clinical Studies (14.3)].

1.4 Acute Bacterial Sinusitis: 5-day and 10-14 day Treatment Regimens
LEVAQUIN® is indicated for the treatment of acute bacterial sinusitis due to Streptococcus pneumoniae, Haemophilus influenzae, or Moraxella catarrhalis [see Clinical Studies (14.4)].
LEVAQUIN® (levofloxacin)

1.5 Acute Bacterial Exacerbation of Chronic Bronchitis
LEVAQUIN® is indicated for the treatment of acute bacterial exacerbation of chronic bronchitis due to methicillin-susceptible Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Haemophilus parainfluenzae, or Moraxella catarrhalis.

1.6 Complicated Skin and Skin Structure Infections
LEVAQUIN® is indicated for the treatment of complicated skin and skin structure infections due to methicillin-susceptible Staphylococcus aureus, Enterococcus faecalis, Streptococcus pyogenes, or Proteus mirabilis [see Clinical Studies (14.5)].

1.7 Uncomplicated Skin and Skin Structure Infections
LEVAQUIN® is indicated for the treatment of uncomplicated skin and skin structure infections (mild to moderate) including abscesses, cellulitis, furuncles, impetigo, pyoderma, wound infections, due to methicillin-susceptible Staphylococcus aureus, or Streptococcus pyogenes.

1.8 Chronic Bacterial Prostatitis
LEVAQUIN® is indicated for the treatment of chronic bacterial prostatitis due to Escherichia coli, Enterococcus faecalis, or methicillin-susceptible Staphylococcus epidermidis [see Clinical Studies (14.8)].

1.9 Complicated Urinary Tract Infections: 5-day Treatment Regimen
LEVAQUIN® is indicated for the treatment of complicated urinary tract infections due to Escherichia coli, Klebsiella pneumoniae, or Proteus mirabilis [see Clinical Studies (14.7)].

1.10 Complicated Urinary Tract Infections: 10-day Treatment Regimen
LEVAQUIN® is indicated for the treatment of complicated urinary tract infections (mild to moderate) due to Enterococcus faecalis, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, or Pseudomonas aeruginosa [see Clinical Studies (14.8)].

1.11 Acute Pyelonephritis: 5 or 10-day Treatment Regimen
LEVAQUIN® is indicated for the treatment of acute pyelonephritis caused by Escherichia coli, including cases with concurrent bacteremia [see Clinical Studies (14.7, 14.8)].

1.12 Uncomplicated Urinary Tract Infections
LEVAQUIN® is indicated for the treatment of uncomplicated urinary tract infections (mild to moderate) due to Escherichia coli, Klebsiella pneumoniae, or Staphylococcus saprophyticus.

1.13 Inhalational Anthrax (Post-Exposure)
LEVAQUIN® is indicated for inhalational anthrax (post-exposure) to reduce the incidence or progression of disease following exposure to aerosolized Bacillus anthracis. The effectiveness of LEVAQUIN® is based on plasma concentrations achieved in humans, a surrogate endpoint reasonably likely to predict clinical benefit. LEVAQUIN® has not been tested in humans for the post-exposure prevention of inhalation anthrax. The safety of LEVAQUIN® in adults for durations of therapy beyond 28 days or in pediatric patients for durations of therapy beyond 14 days has not been studied. Prolonged LEVAQUIN® therapy should only be used when the benefit outweighs the risk [see Dosage and Administration (2.1, 2.2) and Clinical Studies (14.9)].

2 DOSAGE AND ADMINISTRATION

2.1 Dosage in Adult Patients with Normal Renal Function
The usual dose of LEVAQUIN® Tablets or Oral Solution is 250 mg, 500 mg, or 750 mg administered orally every 24 hours, as indicated by infection and described in Table 1.

The usual dose of LEVAQUIN® Injection is 250 mg or 500 mg administered by slow infusion over 60 minutes every 24 hours or 750 mg administered by slow infusion over 90 minutes every 24 hours, as indicated by infection and described in Table 1. These recommendations apply to patients with creatinine clearance ≥ 50 mL/min. For patients with creatinine clearance <50 mL/min, adjustments to the dosing regimen are required [see Dosage and Administration (2.3)].

Table 1: Dosage in Adult Patients with Normal Renal Function (creatinine clearance ≥ 50 mL/min)

<table>
<thead>
<tr>
<th>Type of Infection*</th>
<th>Dosed Every 24 hours</th>
<th>Duration (days)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nosocomial Pneumonia</td>
<td>750 mg</td>
<td>7-14</td>
</tr>
<tr>
<td>Community Acquired Pneumonia</td>
<td>500 mg</td>
<td>7-14</td>
</tr>
<tr>
<td>Community Acquired Pneumonia</td>
<td>750 mg</td>
<td>5</td>
</tr>
<tr>
<td>Acute Bacterial Sinusitis</td>
<td>750 mg</td>
<td>5</td>
</tr>
<tr>
<td>Acute Bacterial Sinusitis</td>
<td>500 mg</td>
<td>10-14</td>
</tr>
<tr>
<td>Acute Bacterial Exacerbation of Chronic Bronchitis</td>
<td>500 mg</td>
<td>7</td>
</tr>
<tr>
<td>Complicated Skin and Skin Structure Infections (SSSI)</td>
<td>750 mg</td>
<td>7-14</td>
</tr>
<tr>
<td>Uncomplicated SSSI</td>
<td>750 mg</td>
<td>7-10</td>
</tr>
<tr>
<td>Chronic Bacterial Prostatitis</td>
<td>500 mg</td>
<td>28</td>
</tr>
<tr>
<td>Complicated Urinary Tract Infection (cUTI) or Acute Pyelonephritis (AP)*</td>
<td>750 mg</td>
<td>5</td>
</tr>
<tr>
<td>Complicated Urinary Tract Infection (cUTI) or Acute Pyelonephritis (AP)*</td>
<td>250 mg</td>
<td>10</td>
</tr>
<tr>
<td>Uncomplicated Urinary Tract Infection</td>
<td>250 mg</td>
<td>3</td>
</tr>
</tbody>
</table>

* Due to the designated pathogens [see Indications and Usage (1.7)].
† Sequential therapy (intravenous to oral) may be instituted at the discretion of the physician.

LEVAQUIN® (levofloxacin)

1. Due to methicillin-susceptible Staphylococcus aureus, Streptococcus pneumoniae (including multi-drug-resistant strains [MDRSP]), Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Chlamydia pneumoniae, Legionella pneumophila, or Mycoplasma pneumoniae [see Indications and Usage (1.3)].

2. Due to Streptococcus pneumoniae (excluding multi-drug-resistant strains [MDRSP]), Haemophilus influenzae, Haemophilus parainfluenzae, Mycoplasma pneumoniae, or Chlamydia pneumoniae [see Indications and Usage (1.3)].

This regimen is indicated for cUTI due to Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis and AP due to E. coli, including cases with concurrent bacteremia.

This regimen is indicated for cUTI due to Enterococcus faecalis, Enterococcus cloacae, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, and for AP due to E. coli.

Drug administration should begin as soon as possible after suspected or confirmed exposure to aerosolized B. anthracis. This indication is based on a surrogate endpoint. Levofloxacin plasma concentrations achieved in humans are reasonably likely to predict clinical benefit [see Clinical Studies (14.9)].

The safety of LEVAQUIN® in adults for durations of therapy beyond 28 days or in pediatric patients for durations beyond 14 days has not been studied. An increased incidence of musculoskeletal adverse events compared to controls has been observed in pediatric patients [see Warnings and Precautions (5.9), Use in Specific Populations (8.4), and Clinical Studies (14.9)]. Prolonged LEVAQUIN® therapy should only be used when the benefit outweighs the risk.

2.2 Dosage in Pediatric Patients
The dosage in pediatric patients ≥ 6 months of age is described below in Table 2.

Table 2: Dosage in Pediatric Patients ≥ 6 months of age

<table>
<thead>
<tr>
<th>Type of Infection*</th>
<th>Dose</th>
<th>Freq. Once every</th>
<th>Duration†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalational Anthrax (post-exposure)§</td>
<td>500 mg</td>
<td>24 hr</td>
<td>60 days§</td>
</tr>
<tr>
<td>Pediatric patients &gt; 50 kg and ≥ 6 months of age</td>
<td>8 mg/kg (not to exceed 250 mg per dose)</td>
<td>12 hr</td>
<td>60 days§</td>
</tr>
</tbody>
</table>

* Due to Bacillus anthracis [see Indications and Usage (1.13)].
† Sequential therapy (intravenous to oral) may be instituted at the discretion of the physician.
‡ Drug administration should begin as soon as possible after suspected or confirmed exposure to aerosolized B. anthracis. This indication is based on a surrogate endpoint. Levofloxacin plasma concentrations achieved in humans are reasonably likely to predict clinical benefit [see Clinical Studies (14.9)].
§ The safety of LEVAQUIN® in pediatric patients for durations of therapy beyond 14 days has not been studied. An increased incidence of musculoskeletal adverse events compared to controls has been observed in pediatric patients [see Warnings and Precautions (5.9), Use in Specific Populations (8.4), and Clinical Studies (14.9)].
¶ Prolonged LEVAQUIN® therapy should only be used when the benefit outweighs the risk.

2.3 Dosage Adjustment in Adults with Renal Impairment
Administer LEVAQUIN® with caution in the presence of renal insufficiency. Careful clinical observation and appropriate laboratory studies should be performed prior to and during therapy since elimination of levofloxacin may be reduced.

No adjustment is necessary for patients with a creatinine clearance ≥ 50 mL/min.

In patients with impaired renal function (creatinine clearance <50 mL/min), adjustment of the dosing regimen is necessary to avoid the accumulation of levofloxacin due to decreased clearance [see Use in Specific Populations (8.6)].

Table 3 shows how to adjust dose based on creatinine clearance.

Table 3: Dosage Adjustment in Adult Patients with Renal Impairment (creatinine clearance < 50 mL/min)

<table>
<thead>
<tr>
<th>Dose in Normal Renal Function Every 24 hours</th>
<th>Creatinine Clearance 20 to 49 mL/min</th>
<th>Creatinine Clearance 10 to 19 mL/min</th>
<th>Hemodialysis or Chronic Ambulatory Peritoneal Dialysis (CAPD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>750 mg</td>
<td>750 mg every 48 hours</td>
<td>750 mg initial dose, then 500 mg every 48 hours</td>
<td>750 mg initial dose, then 500 mg every 48 hours</td>
</tr>
<tr>
<td>500 mg</td>
<td>500 mg initial dose, then 250 mg every 24 hours</td>
<td>500 mg initial dose, then 250 mg every 48 hours</td>
<td>500 mg initial dose, then 250 mg every 48 hours</td>
</tr>
<tr>
<td>250 mg</td>
<td>250 mg every 48 hours</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Due to the designated pathogens [see Indications and Usage (1.7)].
† Sequential therapy (intravenous to oral) may be instituted at the discretion of the physician.
LEVAQUIN® (levofloxacin)

2.4 Drug Interaction With Chelation Agents: Antacids, Sucralfate, Metal Cations, Multivitamins

LEVAQUIN® Tablets and Oral Solution

LEVAQUIN® Tablets and Oral Solution should be administered at least two hours before or two hours after antacids containing magnesium, aluminum, as well as sucralfate, metal cations such as iron, and multivitamin preparations with zinc or didanosine. The concentration of the resulting diluted solution should be 5 mg/mL prior to chewable/buffered tablets or the pediatric powder for oral solution [see Drug Interactions (7.1) and Patient Counseling Information (17.2)].

LEVAQUIN® Injection

LEVAQUIN® Injection should not be co-administered with any solution containing multivalent cations, e.g., magnesium, through the same intravenous line [see Dosage and Administration (2.6)].

2.5 Administration Instructions

Forcible and LEVAQUIN® Tablets, Oral Solution, and Injection

LEVAQUIN® Tablets can be administered without regard to food. It is recommended that LEVAQUIN® Oral Solution be taken 1 hour before or 2 hours after eating.

LEVAQUIN® Injection

Caution: Rapid or bolus intravenous infusion of LEVAQUIN® has been associated with hypotension and must be avoided. LEVAQUIN® Injection should be infused intravenously slowly over a period of not less than 60 or 90 minutes, depending on the dosage. LEVAQUIN® Injection should be administered only by intravenous infusion. It is not for intramuscular, intrathecal, intraperitoneal, or subcutaneous administration.

Hydration for Patients Receiving LEVAQUIN® Tablets, Oral Solution, and Injection

Adequate hydration of patients receiving oral or intravenous LEVAQUIN® should be maintained to prevent the formation of highly concentrated urine. Crystalluria and cylindruria have been reported with quinolones [see Adverse Reactions (6.1) and Patient Counseling Information (17.2)].

2.6 Preparation of Intravenous Product

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Because only limited data are available on the compatibility of LEVAQUIN® Injection with other intravenous substances, additives or other medications should not be added to LEVAQUIN® Injection Premix in Single-Use Flexible Containers and LEVAQUIN® Injection in Single-Use Vials, or infused simultaneously through the same intravenous line. If the same intravenous line is used for sequential infusion of several different drugs, the line should be flushed before and after infusion of LEVAQUIN® Injection with an infusion solution compatible with LEVAQUIN® Injection and with any other drugs administered via this common line.

LEVAQUIN® Injection in Single-Use Vials

Single-use vials require dilution prior to administration.

LEVAQUIN® Injection is supplied in single-use vials containing a concentrated levofloxacin solution with the equivalent of 500 mg (20 mL vial) and 750 mg (30 mL vial) of levofloxacin in Water for Injection, USP. The 20 mL and 30 mL vials each contain 25 mg/mL levofloxacin. These LEVAQUIN® Injection single-use vials must be further diluted with an appropriate solution prior to intravenous administration [see Table 4]. The concentration of the resulting diluted solution should be 5 mg/mL prior to administration.

Compatible Intravenous Solutions: Any of the following intravenous solutions may be used to prepare a 5 mg/mL levofloxacin solution with the approximate pH values:

<table>
<thead>
<tr>
<th>Intravenous Fluids</th>
<th>Final pH of LEVAQUIN® Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% Sodium Chloride Injection, USP</td>
<td>4.54</td>
</tr>
<tr>
<td>5% Dextrose Injection, USP</td>
<td>4.58</td>
</tr>
<tr>
<td>5% Dextrose/0.9% NaCl Injection</td>
<td>4.62</td>
</tr>
<tr>
<td>5% Dextrose in Lactated Ringers</td>
<td>4.52</td>
</tr>
<tr>
<td>Plasma-Lyte 56/5% Dextrose Injection</td>
<td>5.03</td>
</tr>
<tr>
<td>5% Dextrose, 0.45% Sodium Chloride, and 0.15% Potassium Chloride Injection</td>
<td>4.61</td>
</tr>
<tr>
<td>Sodium Lactate Injection (M/6)</td>
<td>5.54</td>
</tr>
</tbody>
</table>

Since no preservative or bacteriostatic agent is present in this product, aseptic technique must be used in preparation of the final intravenous solution. Since the vials are for single-use only, any unused portion remaining in the vial should be discarded. When used to prepare two 250 mg doses from the 20 mL vial containing 500 mg of levofloxacin, the full content of the vial should be withdrawn at once using a single-entry procedure, and a second dose should be prepared and stored for subsequent use [see Stability of LEVAQUIN® Injection Following Dilution].

Prepare the desired dosage of levofloxacin according to Table 5:

<table>
<thead>
<tr>
<th>Desired Dosage</th>
<th>From Appropriate Vial</th>
<th>Volume of Diluent</th>
<th>Infusion Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 mg</td>
<td>10 mL (20 mL Vial)</td>
<td>40 mL</td>
<td>60 min</td>
</tr>
<tr>
<td>500 mg</td>
<td>20 mL (30 mL Vial)</td>
<td>80 mL</td>
<td>60 min</td>
</tr>
<tr>
<td>750 mg</td>
<td>30 mL (30 mL Vial)</td>
<td>120 mL</td>
<td>90 min</td>
</tr>
</tbody>
</table>

For example, to prepare a 500 mg dose using the 20 mL vial (25 mg/mL), withdraw 20 mL and dilute with a compatible intravenous solution to a total volume of 100 mL.

LEVAQUIN® (levofloxacin)

This intravenous drug product should be inspected visually for particulate matter prior to administration. Samples containing visible particles should be discarded.

Stability of LEVAQUIN® Injection Following Dilution: LEVAQUIN® Injection, when diluted in a compatible intravenous fluid to a concentration of 5 mg/mL, is stable for 72 hours when stored at or below 25°C (77°F) and for 14 days when stored under refrigeration at 2°C to 8°C (36°F to 46°F) in plastic intravenous containers. Solutions that are diluted in a compatible intravenous solution and frozen in glass bottles or plastic intravenous containers are stable for 6 months when stored at -20°C (-4°F). Thaw frozen solutions at room temperature 25°C (77°F) or in a refrigerator 8°C (46°F). Do not force thaw by microwave irradiation or water bath immersion. Do not refreeze after initial thawing.

LEVAQUIN® Injection Premix in Single-Use Flexible Containers (5 mg/mL)

LEVAQUIN® Injection is also supplied in flexible containers within a foil overwrap. The premix contains a premixed, ready to use levofloxacin solution in 5% dextrose (D5W) for single-use. The 100 mL premixed flexible containers contain either 250 mg/50 mL or 500 mg/100 mL of levofloxacin solution. The 150 mL flexible container contains 750 mg/150 mL of levofloxacin solution. The concentration of each container is 5 mg/mL. No further dilution of these preparations is necessary. Because the premixed flexible containers are for single-use only, any unused portion should be discarded.

Instructions for the Use of LEVAQUIN® Injection Premix in Flexible Containers:

1. Tear outer wrapper at the notch and remove solution container.
2. Check the container for minute leaks by squeezing the inner bag firmly. If leaks are found, or if the seal is not intact, discard the solution, as the sterility may be compromised.
3. Do not use if the solution is cloudy or a precipitate is present.
4. Use sterile equipment.
5. WARNING: Do not use flexible containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is complete.

Preparation for Administration:

1. Close flow control clamp of administration set.
2. Remove cover from port at bottom of container.
3. Insert piercing pin of administration set into port with a twisting motion until the pin is firmly seated.
4. Suspend container from hanger.
5. Squeeze and release drip chamber to establish proper fluid level in chamber during infusion of LEVAQUIN® Injection Premix in Flexible Containers.
6. Open flow control clamp to expel air from set. Close clamp.
7. Regulate rate of administration with flow control clamp.

3 DOSAGE FORMS AND STRENGTHS

TABLETS, Film-coated, capsule-shaped

- 250 mg terra cotta pink tablets, imprinted with “250” on one side and “LEVAQUIN” on the other
- 500 mg peach tablets, imprinted with “500” on one side and “LEVAQUIN” on the other
- 750 mg white tablets, imprinted with “750” on one side and “LEVAQUIN” on the other
- ORAL SOLUTION, 25mg/mL, clear yellow to clear greenish-yellow color

INJECTION, Single-Use Vials of concentrated solution for dilution for intravenous infusion, clear yellow to clear colorless

INJECTION (5 mg/mL in 5% Dextrose) Premix in Single-Use Flexible Containers, for intravenous infusion

- 100 mL container, fill volume 50 mL (equivalent to 250 mg levofloxacin)
- 100 mL container, fill volume 100 mL (equivalent to 500 mg levofloxacin)
- 150 mL container, fill volume 150 mL (equivalent to 750 mg levofloxacin)

4 CONTRAINDICATIONS

LEVAQUIN® is contraindicated in persons with known hypersensitivity to levofloxacin, or other quinolone antibacterials [see Warnings and Precautions (5.2)].

5 WARNINGS AND PRECAUTIONS

5.1 Tendinopathy and Tendon Rupture

Fluoroquinolones, including LEVAQUIN®, are associated with an increased risk of tendinitis and tendon rupture in all ages. This adverse reaction most frequently involves the Achilles tendon, and rupture of the Achilles tendon may require surgical repair. Tendinitis and tendon rupture in the rotator cuff (the shoulder), the hand, the biceps, the thumb, and other tendon sites have also been reported. The risk of developing fluoroquinolone-associated tendinitis and tendon rupture is further increased in older patients usually over 60 years of age, in those taking corticosteroid drugs, in patients with kidney, heart or lung transplants. Factors, in addition to age and corticosteroid therapy, that may independently increase the risk of tendon rupture include strenuous physical activity, renal failure, and previous tendon disorders such as rheumatoid arthritis. Tendinitis and tendon rupture have been reported in patients taking fluoroquinolones who do not have the above risk factors. Tendon rupture can occur during or after completion of therapy; cases occurring up to several months after completion of therapy have been reported. LEVAQUIN® should be discontinued if the patient experiences pain, swelling, inflammation or rupture of a tendon. Patients should be advised to rest at the first sign of tendinitis or tendon rupture, and to contact their healthcare provider regarding changing to a non-quinolone antimicrobial drug. [see Adverse Reactions (10.3); Patient Counseling Information (17.3)].
5.2 Hypersensitivity Reactions
Serious and occasionally fatal hypersensitivity and/or anaphylactic reactions have been reported in patients receiving therapy with fluoroquinolones, including LEVAQUIN®. These reactions may occur following the administration of multiple doses. Clinical manifestations may include one or more of the following:

- fever, rash, or severe dermatologic reactions (e.g., toxic epidermal necrolysis, Stevens-Johnson Syndrome);
- vasculitis; arthralgia; myalgia; serum sickness;
- allergic pneumonitis;
- interstitial nephritis; acute renal insufficiency or failure;
- hepatitis; jaundice; acute hepatic necrosis or failure;
- anemia, including hemolytic and aplastic; thrombocytopenia, including thrombotic thrombocytopenic purpura; leukopenia; agranulocytosis; pancytopenia; and/or other hematologic abnormalities.

The drug should be discontinued immediately at the first appearance of skin rash, jaundice, or any other sign of hypersensitivity and supportive measures instituted [see Adverse Reactions (6); Patient Counseling Information (17.3)].

5.3 Other Serious and Sometimes Fatal Reactions
Other serious and sometimes fatal events, some due to hypersensitivity, and some due to uncertain etiology, have been reported rarely in patients receiving therapy with fluoroquinolones, including LEVAQUIN®. These events may be severe and generally occur following the administration of multiple doses. Clinical manifestations may include one or more of the following:

5.4 Hepatotoxicity
Post-marketing reports of severe hepatotoxicity (including acute hepatitis and fatal events) have been received for patients treated with LEVAQUIN®. No evidence of serious drug-associated hepatotoxicity was detected in clinical trials of over 7,000 patients. Severe hepatotoxicity generally occurred within 14 days of initiation of therapy and most cases occurred within 6 days. Most cases of severe hepatotoxicity were not associated with hypersensitivity [see Warnings and Precautions (5.3)].

5.5 Central Nervous System Effects
Convulsions and toxic psychoses have been reported in patients receiving fluoroquinolones, including LEVAQUIN®. Fluoroquinolones may also cause increased intracranial pressure and central nervous system stimulation which may lead to tremors, restlessness, hyperactivity, confusion, hallucinations, paranoia, depression, nightmares, insomnia, and, rarely, suicidal thoughts or acts. These reactions may occur following the first dose. If these reactions occur in patients receiving LEVAQUIN®, the drug should be discontinued and appropriate measures instituted. As with other fluoroquinolones, LEVAQUIN® should be used with caution in patients with known hypersensitivity reactions [see Warnings and Precautions (6.3)].

5.6 Clostridium difficile-Associated Diarrhea
Clostridium difficile-associated diarrhea (CDAD) has been reported with nearly all antibacterial agents, including LEVAQUIN®, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections may be refractory to antibiotic therapy and may require colostomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months following the administration of an antibiotic agent.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated [see Adverse Reactions (6.2); Patient Counseling Information (17.3)].

5.7 Peripheral Neuropathy
Rare cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesia, dysesthesias and weakness have been reported in patients receiving fluoroquinolones, including LEVAQUIN®. LEVAQUIN® should be discontinued if the patient experiences symptoms of neuropathy including pain, burning, tingling, numbness, and/or weakness or other alterations of sensation including light touch, pain, temperature, position sense, and vibratory sensation in order to prevent the development of an irreversible condition [see Adverse Reactions (6); Patient Counseling Information (17.3)].

5.8 Prolongation of the QT Interval
Some fluoroquinolones, including LEVAQUIN®, have been associated with prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia. Rare cases of torsade de points have been spontaneously reported during postmarketing surveillance in patients receiving fluoroquinolones, including LEVAQUIN®. LEVAQUIN® should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, and patients receiving Class IA (quinidine, procainamide), or Class III (amiodarone, sotalol) antiarrhythmic agents. Elderly patients may be more susceptible to drug-associated effects on the QT interval [see Adverse Reactions (6.3); Use in Specific Populations (8.5); and Patient Counseling Information (17.3)].

5.9 Musculoskeletal Disorders in Pediatric Patients and Arthropathic Effects in Animals
LEVAQUIN® is indicated in pediatric patients (≥ 6 months of age) only for the prevention of inhalational anthrax (post-exposure) [see Indications and Usage (1.13)]. An increased incidence of musculoskeletal disorders (arthritis, arthralgia, tendinopathy, and gait abnormality) compared to controls has been observed in pediatric patients receiving LEVAQUIN® [see Use in Specific Populations (8.4)].

5.10 Blood Glucose Disturbances
As with other fluoroquinolones, disturbances of blood glucose, including symptomatic hyper- and hypoglycemia, have been reported with LEVAQUIN®, usually in diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (e.g., glyburide) or with insulin. In these patients, careful monitoring of blood glucose is recommended. If a hypoglycemic reaction occurs in a patient being treated with LEVAQUIN®, LEVAQUIN® should be discontinued and appropriate therapy should be initiated immediately [see Adverse Reactions (6.2); Drug Interactions (7.3); Patient Counseling Information (17.4)].

5.11 Photosensitivity/Phototoxicity
Moderate to severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions (e.g., burning, erythema, exudation, vesicles, blistering, edema) involving areas exposed to light (typically the face, “V” area of the neck, extensor surfaces of the forearms, dorsa of the hands), can be associated with the use of fluoroquinolones after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Drug therapy should be discontinued if photosensitivity/phototoxicity occurs [see Adverse Reactions (6.3); Patient Counseling Information (17.3)].

5.12 Development of Drug Resistant Bacteria
Prescribing LEVAQUIN® in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria [see Patient Counseling Information (17.1)].

6. ADVERSE REACTIONS
6.1 Serious and Otherwise Important Adverse Reactions
The following serious and otherwise important adverse drug reactions are discussed in greater detail in other sections of labeling:

- Tendon Effects [see Warnings and Precautions (5.1)];
- Hypersensitivity Reactions [see Warnings and Precautions (5.2)];
- Other Serious and Sometimes Fatal Reactions [see Warnings and Precautions (5.3)];
- Hepatotoxicity [see Warnings and Precautions (5.4)];
- Central Nervous System Effects [see Warnings and Precautions (5.5)];
- Clarithromycin-difficile-Associated Diarrhea [see Warnings and Precautions (5.6)];
- Peripheral Neuropathy [see Warnings and Precautions (5.7)];
- Prolongation of the QT Interval [see Warnings and Precautions (5.8)];
- Musculoskeletal Disorders in Pediatric Patients [see Warnings and Precautions (5.9)];
- Blood Glucose Disturbances [see Warnings and Precautions (5.10)];
- Photosensitivity/Phototoxicity [see Warnings and Precautions (5.11)];
- Development of Drug Resistant Bacteria [see Warnings and Precautions (5.12)].

Hypotension has been associated with rapid or bolus intravenous infusion of LEVAQUIN®. LEVAQUIN® should be infused slowly over 60 to 90 minutes, depending on dosage [see Dosage and Administration (2.6)].
**LEVAQUIN® (levofloxacin)**

Crystalluria and cylindruria have been reported with quinolones, including LEVAQUIN®. Therefore, adequate hydration of patients receiving LEVAQUIN® should be maintained to prevent the formation of a highly concentrated urine [see Dosage and Administration (2.5)].

### 6.2 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to LEVAQUIN® in 7537 patients in 29 pooled Phase 3 clinical trials. The population studied had a mean age of 50 years (approximately 74% of the population was < 65 years of age), 50% were male, 71% were Caucasian, 19% were Black. Patients were treated with LEVAQUIN® for a wide variety of infectious diseases [see Indications and Usage (1)]. Patients received LEVAQUIN® dosages of 750 mg once daily, 250 mg once daily, or 500 mg once or twice daily. Treatment duration was usually 3-14 days, and the mean number of days on therapy was 10 days.

The overall incidence, type and distribution of adverse reactions was similar in patients receiving LEVAQUIN® dosages of 750 mg once daily, 250 mg once daily, and 500 mg once or twice daily. Discontinuation of LEVAQUIN® due to adverse drug reactions occurred in 4.3% of patients overall, 3.8% of patients treated with the 250 mg and 500 mg doses and 5.4% of patients treated with the 750 mg dose. The most common adverse drug reactions leading to discontinuation with the 250 and 500 mg doses were gastrointestinal (1.4%), primarily nausea (0.6%); vomiting (0.4%); dizziness (0.3%); and headache (0.2%). The most common adverse drug reactions leading to discontinuation with the 750 mg dose were gastrointestinal (11.2%), primarily nausea (0.6%), vomiting (0.5%); dizziness (0.3%); and headache (0.3%).

Adverse reactions occurring in ≥ 1% of LEVAQUIN®-treated patients and less common adverse reactions, occurring in 0.1 to <1% of LEVAQUIN®-treated patients, are shown in Table 6 and Table 7, respectively. The most common adverse drug reactions (≥ 3%) are nausea, headache, diarrhea, insomnia, constipation, and dizziness.

#### Table 6: Common (≥ 1%) Adverse Reactions Reported in Clinical Trials with LEVAQUIN®

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>Adverse Reaction</th>
<th>% (N=7537)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and Infestations</td>
<td>moniliasis</td>
<td>1</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td>insomnia* [see Warnings and Precautions (5.5)]</td>
<td>4</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>headache</td>
<td>6</td>
</tr>
<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
<td>dyspnea [see Warnings and Precautions (5.2)]</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>nausea</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>diarrhea</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>constipation</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>abdominal pain</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>vomiting</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>dyspepsia</td>
<td>2</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td>rash [see Warnings and Precautions (5.2)]</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>pruritus</td>
<td>1</td>
</tr>
<tr>
<td>Reproductive System and Breast Disorders</td>
<td>vaginitis</td>
<td>1</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td>edema</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>injection site reaction</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>chest pain</td>
<td>1</td>
</tr>
</tbody>
</table>

* N = 7274

1 N=3758 (women)

#### Table 7: Less Common (0.1 to 1%) Adverse Reactions Reported in Clinical Trials with LEVAQUIN® (N=7537)

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and Infestations</td>
<td>genitai moniliasis</td>
</tr>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td>anemia</td>
</tr>
<tr>
<td></td>
<td>thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td>granulocytopenia</td>
</tr>
<tr>
<td>Immune System Disorders</td>
<td>allergic reaction [see Warnings and Precautions (5.3)]</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td>hyperglycemia</td>
</tr>
<tr>
<td></td>
<td>hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>[see Warnings and Precautions (5.10)]</td>
</tr>
<tr>
<td></td>
<td>hyperkalemia</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td>anxiety</td>
</tr>
<tr>
<td></td>
<td>agitation</td>
</tr>
<tr>
<td></td>
<td>confusion</td>
</tr>
<tr>
<td></td>
<td>depression</td>
</tr>
<tr>
<td></td>
<td>hallucination</td>
</tr>
<tr>
<td></td>
<td>nightmare* [see Warnings and Precautions (5.5)]</td>
</tr>
<tr>
<td></td>
<td>sleep disorder*</td>
</tr>
<tr>
<td></td>
<td>anorexia</td>
</tr>
<tr>
<td></td>
<td>abnormal dreaming*</td>
</tr>
</tbody>
</table>

**LEVAQUIN® (levofloxacin)**

| Nervous System Disorders             | tremor                                    |
|                                      | convulsions                               |
|                                      | paresthesia                               |
|                                      | vertigo                                   |
|                                      | hypotension                               |
|                                      | hyperkinesias                             |
|                                      | abnormal gait                             |
|                                      | somnolence*                               |
|                                      | syncope                                   |

| Respiratory, Thoracic and Mediastinal Disorders | epistaxis                                |
| Cardiac Disorders                       | cardiac arrest                            |
|                                      | palpitation                               |
|                                      | ventricular tachycardia                   |
|                                      | ventricular arrhythm                      |

| Gastrointestinal Disorders            | gastritis                                  |
|                                      | stomatitis                                |
|                                      | pancreatitis                              |
|                                      | esophagitis                               |
|                                      | gastroenteritis                           |
|                                      | glossitis                                 |
|                                      | pseudomembranous/ C. difficile colitis    |

| Hepatobiliary Disorders               | abnormal hepatic function                 |
|                                      | increased hepatic enzymes                 |
|                                      | increased alkaline phosphatase            |

| Skin and Subcutaneous Tissue Disorders | urticaria [see Warnings and Precautions (5.2)] |

| Musculoskeletal and Connective Tissue Disorders | arthralgia                                 |
|                                              | tendonitis                                 |
|                                              | [see Warnings and Precautions (5.1)]       |
|                                              | myalgia                                    |
|                                              | skeletal pain                             |

| Renal and Urinary Disorders            | abnormal renal function                   |
|                                      | acute renal failure [see Warnings and Precautions (5.3)] |

#### Table 8: Postmarketing Reports Of Adverse Drug Reactions

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td>pancytopenia</td>
</tr>
<tr>
<td></td>
<td>aplastic anemia</td>
</tr>
<tr>
<td></td>
<td>leukopenia</td>
</tr>
<tr>
<td></td>
<td>hemolytic anemia</td>
</tr>
<tr>
<td>Immune System Disorders</td>
<td>hypersensitivity reactions, sometimes fatal</td>
</tr>
<tr>
<td></td>
<td>including:</td>
</tr>
<tr>
<td></td>
<td>anaphylactic/anaphylactoid reactions</td>
</tr>
<tr>
<td></td>
<td>anaphylactic shock</td>
</tr>
<tr>
<td></td>
<td>angioneurotic edema</td>
</tr>
<tr>
<td></td>
<td>serum sickness</td>
</tr>
<tr>
<td></td>
<td>[see Warnings and Precautions (5.3)]</td>
</tr>
<tr>
<td></td>
<td>eosinophilia</td>
</tr>
</tbody>
</table>

| Psychiatric Disorders                | psychosis                                  |
|                                      | paranoia                                   |
|                                      | isolated reports of suicide attempt and suicidal ideation [see Warnings and Precautions (5.5)] |

| Nervous System Disorders             | anoxia                                     |
|                                      | aguesia                                   |
|                                      | parosmia                                  |
|                                      | dysgesia                                  |
|                                      | peripheral neuropathy                     |
|                                      | isolated reports of encephalopathy        |

| Eye Disorders                        | vision disturbance, including diplopia  |
|                                      | visual acuity reduced                     |
|                                      | vision blurred                            |
|                                      | scotoma                                   |
**LEVAQUIN® (levofloxacin)**

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Associated Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear and Labyrinth Disorders</td>
<td>hypoacusis</td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td>isolated reports of torsade de pointes electrocardiogram QT prolonged</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td>vasodilatation</td>
</tr>
<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
<td>isolated reports of allergic pneumonitis [see Warnings and Precautions (5.3)]</td>
</tr>
<tr>
<td>Hepatobiliary Disorders</td>
<td>hepatic failure (including fatal cases)</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td>bullous eruptions to include: Stevens-Johnson Syndrome</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td>tendon rupture [see Warnings and Precautions (5.1)]</td>
</tr>
<tr>
<td>Renal and Urinary Disorders</td>
<td>interstitial nephritis [see Warnings and Precautions (5.3)]</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td>multi-organ failure</td>
</tr>
<tr>
<td>Investigations</td>
<td>prothrombin time prolonged</td>
</tr>
</tbody>
</table>

### 7.4 Non-Steroidal Anti-Inflammatory Drugs

The concomitant administration of a non-steroidal anti-inflammatory drug with a fluoroquinolone, including LEVAQUIN®, may increase the risk of gastrointestinal bleeding. No apparent effect of cyclosporine on the plasma concentrations, AUC, and other disposition parameters for cyclosporine was detected in a clinical study involving healthy volunteers. However, elevated plasma levels of cyclosporine were observed when LEVAQUIN® was co-administered with cyclosporine. No significant effect of LEVAQUIN® on the peak plasma concentrations, AUC, and other disposition parameters for cyclosporine was detected in a clinical study involving healthy volunteers. However, elevated plasma levels of cyclosporine were observed when LEVAQUIN® was co-administered with cyclosporine. Adverse reactions, including seizures, may occur with or without an elevation in serum phenytoin levels [see Warnings and Precautions (5.4)].

### 7.6 Cyclosporine

Some fluoroquinolones, including LEVAQUIN®, may produce false-positive urine screening results for opiates using commercially available immunoassay kits. Confirmation of positive opiates screens by more specific methods may be necessary.

### 8 USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy

Pregnancy Category C. Levofloxacin was not teratogenic in rats at oral doses as high as 810 mg/kg/day which corresponds to 3.4 times the highest recommended human dose based upon relative body surface area, or at intravenous doses as high as 160 mg/kg/day corresponding to 1.9 times the highest recommended human dose based upon relative body surface area. The oral dose of 810 mg/kg/day to rats caused decreased fetal body weight and increased fetal mortality. No teratogenicity was observed when rabbits were dosed orally as high as 50 mg/kg/day which corresponds to 1.1 times the highest recommended human dose based upon relative body surface area, or when dosed intravenously as high as 25 mg/kg/day, corresponding to 0.5 times the highest recommended human dose based upon relative body surface area. There are, however, no adequate and well-controlled studies in pregnant women. LEVAQUIN® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

#### 8.3 Nursing Mothers

Based on data on other fluoroquinolones and very limited data on LEVAQUIN®, it can be presumed that levofloxacin will be excreted in human milk. Because of the potential for serious adverse reactions from LEVAQUIN® in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

#### 8.4 Pediatric Use

Quinolones, including levofloxacin, cause arthropathy and osteochondrosis in juvenile animals of several species [see Warnings and Precautions (5.3, 5.4)].

#### 8.5 Interactions with Laboratory or Diagnostic Testing

Confirmation of positive opiate screens by more specific methods may be necessary. Other fluoroquinolones with theophylline has resulted in prolonged elimination half-life, elevated serum theophylline levels, and a subsequent increase in the risk of theophylline-related adverse reactions in the patient population. Therefore, theophylline levels should be closely monitored and appropriate dosage adjustments made when LEVAQUIN® is co-administered. Adverse reactions, including seizures, may occur with or without an elevation in serum theophylline levels [see Warnings and Precautions (5.5)].
LEVAQUIN® (levofloxacin)

Table 9: Incidence of Musculoskeletal Disorders in Pediatric Clinical Trial

<table>
<thead>
<tr>
<th>Follow-up Period</th>
<th>LEVAQUIN®</th>
<th>Non-Fluoroquinolone*</th>
<th>p-value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 days</td>
<td>28 (2.1%)</td>
<td>8 (0.3%)</td>
<td>p = 0.038</td>
</tr>
<tr>
<td>1 year*</td>
<td>46 (3.4%)</td>
<td>16 (1.8%)</td>
<td>p = 0.025</td>
</tr>
</tbody>
</table>

* Non-Fluoroquinolone: ceftriaxone, amoxicillin/clavulanate, clarithromycin
‡ 2-sided Fisher’s Exact Test

8.5 Geriatric Use

Geriatric patients are at increased risk for developing severe tendon rupture when treated with a fluoroquinolone such as LEVAQUIN®. This risk is further increased in patients receiving concomitant corticosteroid therapy. Tendinitis or tendon rupture can involve the Achilles, hand, shoulder, or other tendon sites and can occur during or after completion of therapy; cases occurring up to several months after fluoroquinolone treatment have been reported. Caution should be used when prescribing LEVAQUIN® to elderly patients especially those on corticosteroids. Patients should be informed of this potential side effect and advised to discontinue LEVAQUIN® and contact their healthcare provider if any symptoms of tendinitis or tendon rupture occur.[see Boxed Warning; Warnings and Precautions (5.1); and Adverse Reactions (6.3)].

In phase 3 clinical trials, 1,945 LEVAQUIN®-treated patients (26%) were ≥ 65 years of age. Of these, 1,081 patients (14%) were between the ages of 65 and 74 and 864 patients (12%) were 75 years or older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, but greater sensitivity of some older individuals cannot be ruled out.

Severe, and sometimes fatal, cases of hepatotoxicity have been reported post-marketing in association with LEVAQUIN®. The majority of fatal hepatotoxicity reports occurred in patients 65 years of age or older and most were not associated with hypersensitivity. LEVAQUIN® should be discontinued immediately if the patient develops signs and symptoms of hepatitis.[see Warnings and Precautions (5.4)].

Elderly patients may be more susceptible to drug-associated effects on the QT interval. Therefore, precaution should be taken when using LEVAQUIN® with concomitant drugs that can result in prolongation of the QT interval (e.g., Class IA or Class III antiarrhythmics) or in patients with risk factors for torsade de pointes (e.g., known QT prolongation, uncorrected hypokalemia) [see Warnings and Precautions (5.8)].

The pharmacokinetic properties of levofloxacin in younger adults and elderly adults do not differ significantly when creatinine clearance is taken into consideration. However, since the drug is known to be substantially excreted by the kidney, the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function [see Clinical Pharmacology (12.3)].

11 DESCRIPTION

LEVAQUIN® is a synthetic broad-spectrum antibacterial agent for oral and intravenous administration. Chemically, levofloxacin, a chiral fluorinated carboxyquinoline, is the pure (+)-enantiomer of the racemic drug substance ofloxacin. The chemical name is [(+)-(S)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-þpyridin(1,2-d)-1,4-benzoxazine-6-carboxylic acid hemihydrate. The empirical formula is C_{18}H_{17}F_{2}N_{2}O_{5}·1/2 H_{2}O and the molecular weight is 370.38.

V洛キサシン is a light yellowish-white to yellow-white crystal or crystalline powder. The molecule exists as a zwitterion at the pH conditions in the small intestine.

The data demonstrate that from pH 0.6 to 5.8, the solubility of levofloxacin is essentially constant (approximately 100 mg/mL). Levofloxacin is considered soluble to freely soluble in this pH range, as defined by USP nomenclature. Above pH 5.8, the solubility levofloxacin rapidly decreases to pH 6.7 (272 mg/mL) and is considered freely soluble in this range. Above pH 6.7, the solubility decreases and reaches a minimum value (about 50 mg/mL) at a pH of approximately 6.9.

LEVOKASIN has the potential to form stable coordination compounds with many metal ions. This in vitro chelation potential has the following formation order: Al³⁺<Cu²⁺<Zn²⁺<Mg²⁺<Ca²⁺.

Excipients and Description of Dosage Forms

LEVOKASIN Tablets

LEVOKASIN Tablets are available as film-coated tablets and contain the following inactive ingredients:

- 250 mg (as expressed in the anhydrous form): hypromellose, crospovidone, microcrystalline cellulose, magnesium stearate, polyethylene glycol, titanium dioxide, polysorbate 80 and synthetic red iron oxide.
- 500 mg (as expressed in the anhydrous form): hypromellose, crospovidone, microcrystalline cellulose, magnesium stearate, polyethylene glycol, titanium dioxide, polysorbate 80 and synthetic red and yellow iron oxides.
- 750 mg (as expressed in the anhydrous form): hypromellose, crospovidone, microcrystalline cellulose, magnesium stearate, polyethylene glycol, titanium dioxide, polysorbate 80.

LEVOKASIN Oral Solution

LEVOKASIN Oral Solution, 25 mg/mL, is a multi-use self-preserving aseptic aqueous solution of levofloxacin with pH ranging from 5.6 to 6.0. The appearance of LEVKASIN Oral Solution may range from clear yellow to clear greenish-yellow. This does not adversely affect product potency.

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

LEVOKASIN Injection

The appearance of LEVKASIN Injection may range from a clear yellow to a clear greenish-yellow solution. This does not adversely affect product potency.

LEVOKASIN Injection in Single-Use Vials is a sterile, preservative-free aqueous solution of levofloxacin in Water for Injection, with pH ranging from 3.8 to 5.8.

LEVOKASIN Injection Premix in Single-Use Flexible Containers is a sterile, preservative-free aqueous solution of levofloxacin with pH ranging from 3.8 to 5.8. This is a dilute, non-pyrogenic, nearly isotonic premixed solution that contains levofloxacin in 5% Dextrose (D₅W). Solutions of hydrochloric acid and sodium hydroxide may have been added to adjust the pH.

The flexible container is fabricated from a specially formulated non-plasticized, thermoplastic copolyester (CRS). The amount of water that can permeate from the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the flexible container can leach out certain of the container’s chemical components in very small amounts within the expiration period. The suitability of the container material has been confirmed by tests in animals according to USP biological tests for plastic containers.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

LEVOKASIN is a member of the fluoroquinolone class of antibacterial agents [see Clinical Pharmacology (12.4)].

12.3 Pharmacokinetics

The mean ±SD pharmacokinetic parameters of levofloxacin determined under single and steady-state conditions following oral tablet, oral solution, or intravenous (IV) doses of LEVAQUIN® are summarized in Table 10.
The administration of a 500 mg dose of LEVAQUIN® with food prolongs the time to peak and trough plasma concentrations attained following multiple once-daily IV regimens were approximately 5.7 ± 1.4 and 0.5 ± 0.2 mcg/mL after the 500 mg doses, following a 500 mg or 750 mg once-daily dosage regimen. The mean ± SD peak and trough concentrations were 11.5 ± 4.9° and ND ± 10.4 ± 39.7 ± 13 ND 71.1 ± 19 ND 51.2 ± 24 ND 9.3 ± 1.8 1.6 ± 0.8 101 ± 20 129 ± 24 83 ± 17 7.5 ± 0.9 ND

500 mg IV 7 11.5 ± 4.9° ND 110 ± 40 129 ± 36 75 ± 13 7.5 ± 1.6 ND

Distribution
The mean volume of distribution of levofloxacin generally ranges from 74 to 112 L after single or multiple 500 mg or 750 mg doses, indicating widespread distribution into body tissues. Levofloxacin reaches its peak levels in skin tissues and in blister fluid of healthy subjects at approximately 3 hours after dosing. The skin tissue bioavailability to plasma AUC ratio is approximately 2 and the blister fluid to plasma AUC ratio is approximately 1 following once-daily oral administration of 750 mg and 500 mg doses of LEVAQUIN®

Metabolism
Levofloxacin is stereospecifically stable in plasma and urine and does not invert metabolically to its enantiomer, D-oxofloxacin. Levofloxacin undergoes limited metabolism in humans and is primarily excreted as unchanged drug in the urine. Following oral administration, approximately 83% of an administered dose was recovered as unchanged drug in urine within 48 hours, whereas less than 4% of the dose was recovered in feces in 72 hours. Less than 5% of an administered dose was recovered in the urine as the desmethyl and N-oxide metabolites, the only metabolites identified in humans. These metabolites have little relevant pharmacological activity.

Excretion
Levofloxacin is excreted largely as unchanged drug in the urine. The mean terminal plasma elimination half-life of levofloxacin ranges from approximately 8 to 11 hours following single or multiple doses of levofloxacin given orally or intravenously. The mean apparent total body clearance and renal clearance range from approximately 144 to 226 mL/min and 96 to 142 mL/min, respectively. Renal clearance in excess of the glomerular filtration rate suggests that tubular secretion of levofloxacin occurs in addition to its glomerular filtration. Concomitant administration of either cimetidine or probenecid results in approximately 24% and 35% reduction in the levofloxacin renal clearance, respectively, indicating that secretion of levofloxacin occurs in the renal proximal tubule. No levofloxacin crystals were found in any of the urine samples freshly collected from subjects receiving LEVAQUIN®

Geriatric
There are no significant differences in levofloxacin pharmacokinetics between young elderly subjects when the subjects' differences in creatinine clearance are taken into consideration. Following a 500 mg oral dose of LEVAQUIN® to healthy elderly subjects (66 - 80 years of age), the mean terminal plasma elimination half-life of levofloxacin was about 7.6 hours, as compared to approximately 6 hours in younger adults. The difference was attributable to the variation in renal function status of the subjects and was believed to be clinically significant. Drug absorption appears to be unaffected by age. LEVAQUIN® dose adjustment based on age alone is not necessary [See Use in Specific Populations (8.5)].

Pediatrics
The pharmacokinetics of levofloxacin following a single 7 mg/kg intravenous dose were investigated in pediatric patients ranging in age from 6 months to 16 years. Pediatric patients cleared levofloxacin faster than adult patients, resulting in lower plasma exposures than adults for a given mg/kg dose. Subsequent pharmacokinetic analyses predicted that a dosage regimen of 8 mg/kg every 12 hours (not to exceed 250 mg per dose) for pediatric patients 6 months to 17 years of age would achieve comparable steady state plasma exposures (AUC0-24 and Cmax) to those observed in adult patients administered 500 mg of levofloxacin once every 24 hours.

Gender
There are no significant differences in levofloxacin pharmacokinetics between male and female subjects when subjects' differences in creatinine clearance are taken into consideration. Following a 500 mg oral dose of LEVAQUIN® to healthy male subjects, the mean terminal plasma elimination half-life of levofloxacin was about 7.5 hours, as compared to approximately 6 hours in female subjects. This difference in drug elimination was due to the female gender and female subjects and was not believed to be clinically significant. Drug absorption appears to be unaffected by the gender of the subjects. Dose adjustment based on gender alone is not necessary.

Absorption
Levofloxacin is rapidly and essentially completely absorbed after oral administration. Peak plasma concentrations are usually attained one to two hours after oral dosing. The absolute bioavailability of levofloxacin from a 500 mg tablet and a 750 mg tablet of LEVAQUIN® are both approximately 99%, demonstrating complete oral absorption of levofloxacin. Following a single intravenous dose of LEVAQUIN® to healthy male and female subjects when subjects' differences in creatinine clearance are taken into consideration. Following a 500 mg oral dose of LEVAQUIN® to healthy male subjects (66 - 80 years of age), the mean terminal plasma elimination half-life of levofloxacin was about 7.6 hours, as compared to approximately 6 hours in younger adults. The difference was attributable to the variation in renal function status of the subjects and was believed to be clinically significant. Drug absorption appears to be unaffected by age. LEVAQUIN® dose adjustment based on age alone is not necessary [See Use in Specific Populations (8.5)].

Table: Mean ± SD Levofloxacin PK Parameters

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Tmax (h)</th>
<th>AUC (mcg·h/mL)</th>
<th>CL/F (L/min)</th>
<th>Vd/F (L)</th>
<th>t1/2 (h)</th>
<th>CL (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single dose</td>
<td>2.8 ± 0.4</td>
<td>1.6 ± 1.0</td>
<td>27.2 ± 3.9</td>
<td>156 ± 20</td>
<td>ND</td>
<td>7.3 ± 0.9</td>
</tr>
<tr>
<td>500 mg tablet</td>
<td>5.1 ± 0.8</td>
<td>1.3 ± 0.6</td>
<td>47.9 ± 6.8</td>
<td>178 ± 28</td>
<td>ND</td>
<td>6.3 ± 0.6</td>
</tr>
<tr>
<td>500 mg oral solution</td>
<td>5.8 ± 1.8</td>
<td>0.8 ± 0.7</td>
<td>47.8 ± 10.6</td>
<td>183 ± 40</td>
<td>ND</td>
<td>112 ± 25</td>
</tr>
<tr>
<td>500 mg IV</td>
<td>6.2 ± 1.0</td>
<td>1.0 ± 0.1</td>
<td>48.3 ± 5.4</td>
<td>175 ± 20</td>
<td>ND</td>
<td>6.4 ± 0.7</td>
</tr>
<tr>
<td>750 mg tablet</td>
<td>9.3 ± 1.8</td>
<td>1.6 ± 0.8</td>
<td>101 ± 20</td>
<td>129 ± 24</td>
<td>ND</td>
<td>7.5 ± 0.9</td>
</tr>
<tr>
<td>750 mg IV</td>
<td>11.5 ± 4°</td>
<td>ND</td>
<td>110 ± 40</td>
<td>129 ± 36</td>
<td>ND</td>
<td>7.5 ± 1.6</td>
</tr>
</tbody>
</table>

Absorption
Levofloxacin is rapidly and essentially completely absorbed after oral administration. Peak plasma concentrations are usually attained one to two hours after oral dosing. The absolute bioavailability of levofloxacin from a 500 mg tablet and a 750 mg tablet of LEVAQUIN® is both approximately 99%, demonstrating complete oral absorption of levofloxacin. Following a single intravenous dose of LEVAQUIN® to healthy volunteers, Peak plasma concentrations are usually attained one to two hours after oral dosing. The absolute bioavailability of levofloxacin from a 500 mg tablet and a 750 mg tablet of LEVAQUIN® is both approximately 99%, demonstrating complete oral absorption of levofloxacin. Following a single intravenous dose of LEVAQUIN® to healthy volunteers, Peak plasma concentrations are usually attained one to two hours after oral dosing. The absolute bioavailability of levofloxacin from a 500 mg tablet and a 750 mg tablet of LEVAQUIN® is both approximately 99%, demonstrating complete oral absorption of levofloxacin. Following a single intravenous dose of LEVAQUIN® to healthy volunteers, Peak plasma concentrations are usually attained one to two hours after oral dosing.
LEVAQUIN® (levofloxacin)

Race
The effect of race on levofloxacin pharmacokinetics was examined through a covariate analysis performed on data from 72 subjects: 48 white and 24 non-white. The apparent total body clearance and apparent volume of distribution were not affected by the race of the subjects.

Renal Impairment
Clearance of levofloxacin is substantially reduced and plasma elimination half-life is substantially prolonged in adult patients with impaired renal function [creatinine clearance < 50 mL/min], requiring dosage adjustment in such patients to avoid accumulation. Neither hemodialysis nor continuous ambulatory peritoneal dialysis (CAPD) is effective in removal of levofloxacin from the body, indicating that supplemental doses of LEVAQUIN® are not required following hemodialysis or CAPD [see Dosage and Administration (2.3), Use in Specific Populations (8.6)].

Hepatic Impairment
Pharmacokinetic studies in hepatically impaired patients have not been conducted. Due to the limited extent of levofloxacin metabolism, the pharmacokinetics of levofloxacin are not expected to be affected by hepatic impairment [See Use in Specific Populations (8.7)].

Bacterial Infection
The pharmacokinetics of levofloxacin in patients with serious community-acquired bacterial infections are comparable to those observed in healthy subjects.

Drug-Drug Interactions
The potential for pharmacokinetic drug interactions between LEVAQUIN® and antacids, warfarin, theophylline, cyclosporine, digoxin, probenecid, and cimetidine has been evaluated [see Drug Interactions (7)].

12.4 Microbiology
Mechanism of Action
Levofoxacin is the L-isomer of the racemate, ofloxacin, a quinolone antimicrobial agent. The antibacterial activity of ofloxacin resides primarily in the L-isomer. The mechanism of action of levofloxacin and other fluoroquinolones antimicrobials involves inhibition of bacterial topoisomerase IV and DNA gyrase (both of which are type II topoisomerases), enzymes required for DNA replication, transcription, repair and recombination.

Drug Resistance
Fluoroquinolone resistance can arise through mutations in defined regions of DNA gyrase or topoisomerase IV, termed the Quinolone-Resistance Determining Regions (QRDRs), or through altered efflux. Fluoroquinolones, including levofloxacin, differ in chemical structure and mode of action from aminoglycosides, macrolides and β-lactam antibiotics, including penicillins. Fluoroquinolones may, therefore, be active against bacteria resistant to these antimicrobials.

Resistance to levofloxacin due to spontaneous mutation in vitro is a rare occurrence (range: 10^-9 to 10^-10). Although cross-resistance has been observed between levofloxacin and some other fluoroquinolones, some microorganisms resistant to other fluoroquinolones may be susceptible to levofloxacin.

Activity in vitro and in vivo
Levofoxacin has in vitro activity against a wide range of Gram-negative and Gram-positive microorganisms.

Levofoxacin is often bactericidal at concentrations equal or slightly greater than inhibitory concentrations.

Levofoxacin has been shown to be active against most strains of the following microorganisms both in vitro and in clinical infections as described in Indications and Usage (1).

Aerobic Gram-Positive Microorganisms
Enterococcus faecalis (many strains are only moderately susceptible)
Staphylococcus aureus (methicillin-susceptible strains)
Staphylococcus epidermidis (methicillin-susceptible strains)
Staphylococcus saprophyticus
Streptococcus pneumoniae (including multi-drug resistant strains [MDRSP])
Streptococcus pyogenes

MDRSP (Multi-drug resistant Streptococcus pneumoniae) isolates are strains resistant to two or more of the following antibiotics: penicillin (MIC ≥ 2 mcg/mL), 2nd generation cephalosporins, e.g., cefuroxime; macrolides; tetracyclines and trimethoprim/sulfamethoxazole.

Aerobic Gram-Negative Microorganisms
Enterobacter cloacae
Escherichia coli
Haemophilus influenzae
Haemophilus parainfluenzae
Klebsiella pneumoniae

As with other drugs in this class, some strains of Pseudomonas aeruginosa may develop resistance fairly rapidly during treatment with LEVAQUIN®.

Other Microorganisms
Chlamydia pneumoniae
Mycoplasma pneumoniae

Levofoxacin has been shown to be active against Bacillus anthracis both in vitro and by use of plasma levels as a surrogate marker in a hæsus monkey model for anthrax (post-exposure) [see Indications and Usage (1.13), Clinical Studies (14.9)].

LEVAQUIN® (levofloxacin)
The following in vitro data are available, but their clinical significance is unknown:

Levofoxacin exhibits in vitro minimum inhibitory concentrations (MIC values) of 2 mcg/mL or less against (≥ 90%) strains of the following microorganisms; however, the safety and effectiveness of LEVAQUIN® in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled trials.

Aerobic Gram-Positive Microorganisms
Staphylococcus haemolyticus
(β-hemolytic Streptococcus [Group C/F])
(β-hemolytic Streptococcus [Group G])

Aerobic Gram-Negative Microorganisms
Acinetobacter baumannii
Acinetobacter Iwoffii
Bordetella pertussis
Citrobacter koseri
Citrobacter freundii
Enterobacter aerogenes
Enterobacter sakazakii

Anaerobic Gram-Positive Microorganisms
Clostridium perfringens

Susceptibility Tests
Susceptibility testing for levofloxacin should be performed, as it is the optimal predictor of activity.

- Dilution techniques:
Quantitative methods are used to determine antimicrobial minimal inhibitory concentrations (MIC values). These MIC values provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MIC values should be determined using a standardized procedure. Standardized procedures are based on a dilution method (broth or agar) or equivalent with standardized inoculum concentrations and standardized concentrations of levofloxacin powder. The MIC values should be interpreted according to the criteria outlined in Table 11.

- Diffusion techniques:
Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 5 mcg levofloxacin to test the susceptibility of microorganisms to levofloxacin.

Reports from the laboratory providing results of the standard single-disk susceptibility test with a 5 mcg levofloxacin disk should be interpreted according to the criteria outlined in Table 11. Interpretation involves correlation of the diameter obtained in the disk test with the MIC for levofloxacin.

Table 11: Susceptibility Interpretive Criteria for LEVAQUIN®

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Minimum Inhibitory Concentrations (mcg/mL)</th>
<th>Disk Diffusion (zone diameter in mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriaceae</td>
<td>≤ 2</td>
<td>≤ 4</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>≤ 2</td>
<td>≤ 4</td>
</tr>
<tr>
<td>Methicillin-susceptible Staphylococcus species</td>
<td>≤ 2</td>
<td>≤ 4</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>≤ 2*</td>
<td>≤ 4</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>≤ 2*</td>
<td>≤ 4</td>
</tr>
<tr>
<td>Haemophilus parainfluenzae</td>
<td>≤ 2*</td>
<td>≤ 4</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>≤ 2*</td>
<td>≤ 4</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>≤ 2</td>
<td>≤ 4</td>
</tr>
</tbody>
</table>

S = Susceptible, I = Intermediate, R = Resistant
* These interpretive standards are applicable only to broth microdilution susceptibility testing with Haemophilus influenzae and Haemophilus parainfluenzae using Haemophilus Test Medium.
1 The current absence of data on resistant strains precludes defining any categories other than “Susceptible.” Strains yielding MIC zone diameter results suggestive of a “non-susceptible” category should be submitted to a reference laboratory for further testing.
2 These interpretive standards are applicable only to disk diffusion susceptibility testing with Haemophilus influenzae and Haemophilus parainfluenzae using Haemophilus Test Medium.
3 These zone diameter standards for Streptococcus spp. including S. pneumoniae apply only to tests performed using Mueller-Hinton agar supplemented with 5% sheep blood and incubated in 5% CO2.
4 A report of Susceptible indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of Intermediate indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category also provides a possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where a high dosage of drug can be used. This category also provides a buffer zone which prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of Resistant indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.
14.1 Nosocomial Pneumonia

Adult inpatients and outpatients with a diagnosis of community-acquired bacterial pneumonia were evaluated in 2 pivotal clinical studies. In the first study, 590 patients were enrolled in a prospective, multicenter, unblinded randomized trial comparing LEVAQUIN® 500 mg once orally or intravenously for 7 to 14 days to ceftriaxone 1 to 2 grams intravenously once or in equally divided doses twice daily followed by cefuroxime axetil 500 mg orally twice daily for a total of 7 to 14 days. Patients assigned to treatment with the control regimen were allowed to receive erythromycin (or doxycycline if intolerant of erythromycin) if an infection due to atypical pathogens was suspected or proven. Clinical and microbiologic evaluations were performed during treatment, 5 to 7 days posttherapy, and 3 to 4 weeks posttherapy. Clinical success (cure plus improvement) with LEVAQUIN® at 5 to 7 days posttherapy, the primary efficacy variable for this study was superior (95%) to the control group (83%). The 95% CI for the difference of response rates (LEVAQUIN® minus comparator) was [-17.2, 12.0]. The microbiological eradication rates at the posttherapy visit were 66.7% for LEVAQUIN® and 60.6% for comparator. The 95% CI for the difference of eradication rates (LEVAQUIN® minus comparator) was [-8.3, 20.3]. Clinical success and microbiological eradication rates by pathogen are detailed in Table 13.

### Table 13: Clinical Success Rates and Microbiological Eradication Rates (Nosocomial Pneumonia)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>LEVAQUIN® N (%) of Patients</th>
<th>Microbiologic/ Clinical Outcomes</th>
<th>Imipenem/Cilastatin N (%) of Patients</th>
<th>Microbiologic/ Clinical Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSSA*</td>
<td>21 (146/171)</td>
<td>19 (126/157)</td>
<td>19 (126/157)</td>
<td>18 (115/184)</td>
</tr>
<tr>
<td>P. aeruginosa†</td>
<td>10 (58/11)</td>
<td>7 (52/71)</td>
<td>7 (52/71)</td>
<td>7 (52/71)</td>
</tr>
<tr>
<td>S. marcescens†</td>
<td>11 (91/87)</td>
<td>7 (63/73)</td>
<td>7 (63/73)</td>
<td>7 (63/73)</td>
</tr>
<tr>
<td>E. coli</td>
<td>12 (103/97)</td>
<td>11 (93/87)</td>
<td>10 (93/87)</td>
<td>9 (83/87)</td>
</tr>
<tr>
<td>K. pneumonia‡</td>
<td>9 (81/95)</td>
<td>7 (65/73)</td>
<td>7 (65/73)</td>
<td>7 (65/73)</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>16 (138/138)</td>
<td>15 (129/129)</td>
<td>14 (129/129)</td>
<td>13 (119/119)</td>
</tr>
<tr>
<td>S. pneumonia</td>
<td>4 (370/370)</td>
<td>5 (71/71)</td>
<td>5 (71/71)</td>
<td>5 (71/71)</td>
</tr>
</tbody>
</table>

* Meticillin-susceptible S. aureus
† See above text for use of combination therapy
‡ The observed differences in rates for the clinical and microbiological outcomes may reflect other factors that were not accounted for in the study.
**LEVAQUIN® (levofloxacin)**

**Community-Acquired Pneumonia Due to Multi-Drug Resistant Streptococcus pneumoniae**

LEVAQUIN® was effective for the treatment of community-acquired pneumonia caused by multi-drug resistant Streptococcus pneumoniae (MDRP). MDRP isolates are strains resistant to three or more of the following antibiotics: penicillin (MIC ≥ 2 mcg/mL), 2nd generation cephalosporins (e.g., cefuroxime, macrolides, tetracyclines and trimethoprim/sulfamethoxazole). Of 40 microbiologically evaluable patients with MDRP isolates, 38 patients (95.0%) achieved clinical and bacteriologic success at post-therapy. The clinical and bacterial success rates are shown in Table 15.

**Table 15: Clinical and Bacterial Success Rates for LEVAQUIN*-Treated MDRSP in Community Acquired Pneumonia Patients (Population Valid for Efficacy)**

<table>
<thead>
<tr>
<th>Screening Susceptibility</th>
<th>Clinical Success n/N</th>
<th>Bacteriologic Success n/N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin-resistant</td>
<td>16/17 (94.1%)</td>
<td>16/17 (94.1%)</td>
</tr>
<tr>
<td>2nd generation cephalosporin resistant</td>
<td>31/32 (96.9%)</td>
<td>31/32 (96.9%)</td>
</tr>
<tr>
<td>Macrolide-resistant</td>
<td>28/29 (96.6%)</td>
<td>28/29 (96.6%)</td>
</tr>
<tr>
<td>Trimethoprim/ Sulfamethoxazole resistant</td>
<td>17/19 (90.5%)</td>
<td>17/19 (90.5%)</td>
</tr>
<tr>
<td>Tetracycline-resistant</td>
<td>12/12 (100%)</td>
<td>12/12 (100%)</td>
</tr>
</tbody>
</table>

* One patient had a residual isolate that was resistant to tetracycline, cefuroxime, macrolides and TMP/SMX and intermediate to penicillin and a blood isolate that was intermediate to penicillin and cefuroxime and resistant to the other classes. The patient is included in the database based on isolate resistance.

† n=the number of microbiologically evaluable patients who were clinical successes; N-number of MDRSP isolates eradicated or presumed eradicated in microbiologically evaluable patients; N=number of MDRSP isolates in a designated resistance group.

Not all isolates were resistant to all antimicrobial classes tested. Success and eradication rates are summarized in Table 16.

**Table 16: Clinical Success and Bacteriologic Eradication Rates for Resistant Streptococcus pneumoniae (Community Acquired Pneumonia)**

<table>
<thead>
<tr>
<th>Type of Resistance</th>
<th>Clinical Success</th>
<th>Bacteriologic Eradication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistant to 2 antibacterials</td>
<td>17/18 (94.4%)</td>
<td>17/18 (94.4%)</td>
</tr>
<tr>
<td>Resistant to 3 antibacterials</td>
<td>14/15 (93.3%)</td>
<td>14/15 (93.3%)</td>
</tr>
<tr>
<td>Resistant to 4 antibacterials</td>
<td>7/7 (100%)</td>
<td>7/7 (100%)</td>
</tr>
<tr>
<td>Resistant to 5 antibacterials</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Bacteremia with MDRSP</td>
<td>8/9 (89%)</td>
<td>8/9 (89%)</td>
</tr>
</tbody>
</table>

14.3 Community-Acquired Pneumonia: 5-Day Treatment Regimen

To evaluate the safety and efficacy of higher dose and shorter course of LEVAQUIN®, 528 outpatient and hospitalized adults with clinically and radiologically determined mild to severe community-acquired pneumonia were evaluated in a double-blind, randomized, prospective, multicenter study comparing LEVAQUIN® 750 mg, IV or orally, every day for five days or LEVAQUIN® 500 mg IV or orally once daily for five days.

Clinical success rates (cure plus improvement) in the clinically evaluable population were 90.9% in the LEVAQUIN® 750 mg group and 91.1% in the LEVAQUIN® 500 mg group. The 95% CI for the difference of response rates (LEVAQUIN® 750 minus LEVAQUIN® 500) was [-5.3, 5.4]. In the clinically evaluable population (31-38 days after enrollment) pneumonia was observed in 7 out of 151 patients in the LEVAQUIN® 750 mg group and 2 out of 147 patients in the LEVAQUIN® 500 mg group. Given the small numbers observed, the significance of this finding cannot be determined statistically. The microbiologic efficacy of the 5-day regimen was documented for infections listed in Table 17.

**Table 17: Microbiological Eradication Rates (Community-Acquired Pneumonia)**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>LEVAQUIN® (N=136)</th>
<th>Ciprofloxacin (N=125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pneumoniae</td>
<td>19/20 (95%)</td>
<td>14/15 (93.3%)</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>12/12</td>
<td>11/13 (84.6%)</td>
</tr>
<tr>
<td>Haemophilus parainfluenzae</td>
<td>10/10</td>
<td>10/11 (90.9%)</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>26/27</td>
<td>25/27 (92.6%)</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>13/15</td>
<td>13/13 (100%)</td>
</tr>
</tbody>
</table>

* Eradication rates shown are for patients who had a sole pathogen only; mixed cultures were excluded.

**Table 18: Clinical Success Rate by Pathogen at the TOC in Microbiologically Evaluable Subjects Who Underwent Antral Puncture (Acute Bacterial Sinusitis)**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>LEVAQUIN® (750 mg x 5 days)</th>
<th>LEVAQUIN® (500 mg x 10 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumoniae*</td>
<td>25/27 (92.6%)</td>
<td>26/27 (96.3%)</td>
</tr>
<tr>
<td>Haemophilus influenzae*</td>
<td>19/21 (90.5%)</td>
<td>25/27 (92.6%)</td>
</tr>
<tr>
<td>Moraxella catarrhalis*</td>
<td>10/11 (90.9%)</td>
<td>13/13 (100%)</td>
</tr>
</tbody>
</table>

14.4 Acute Bacterial Sinusitis: 5-day and 10-14 day Treatment Regimens

LEVAQUIN® is approved for the treatment of acute bacterial sinusitis (ABS) using either 750 mg by mouth x 5 days or 500 mg by mouth once daily x 10-14 days. To evaluate the safety and efficacy of a high dose short course of LEVAQUIN®, 789 outpatient adults with clinically and radiologically determined acute bacterial sinusitis were evaluated in a double-blind, randomized, prospective, multicenter study comparing LEVAQUIN® 750 mg by mouth once daily for five days to LEVAQUIN® 500 mg by mouth once daily for 10 days.

Clinical success rates (defined as complete or partial resolution of the pre-treatment signs and symptoms of ABS to such an extent that no further antibiotic treatment was deemed necessary) in the microbiologically evaluable population were 91.4% (139/152) in the LEVAQUIN® 750 mg group and 88.6% (132/149) in the LEVAQUIN® 500 mg group at the test-of-cure (TOC) visit (95% CI [-4.2, 10.0] for LEVAQUIN® 750 mg minus LEVAQUIN® 500 mg).

**Table 19: Microbiological Eradication Rates (Chronic Bacterial Prostatitis)**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>LEVAQUIN® (N=136)</th>
<th>Ciprofloxacin (N=125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>15 (11/136) (81.6%)</td>
<td>15 (13/125) (104.0%)</td>
</tr>
<tr>
<td>E. faecalis</td>
<td>54 (39/125) (72.2%)</td>
<td>44 (32/125) (77.6%)</td>
</tr>
<tr>
<td>S. epidermidis*</td>
<td>11 (9/125) (81.8%)</td>
<td>14 (11/125) (87.6%)</td>
</tr>
</tbody>
</table>

* Eradication rates shown are for patients who had a sole pathogen only; mixed cultures were excluded.

Clinical success (cure + improvement with no need for further antibiotic therapy) rates in microbiologically evaluable population 5-18 days after completion of therapy were 75.0% for LEVAQUIN®-treated patients and 72.8% for ciprofloxacin-treated patients (95% CI [-8.87, 13.27] for LEVAQUIN® minus ciprofloxacin). Clinical long-term success (24-45 days after completion of therapy) rates were 66.7% for the LEVAQUIN®-treated patients and 76.9% for the ciprofloxacin-treated patients (95% CI [-12.98, 28.80] for LEVAQUIN® minus ciprofloxacin).

14.7 Complicated Urinary Tract Infections and Acute Pyelonephritis: 5-day Treatment Regimen

To evaluate the safety and efficacy of the higher dose and shorter course of LEVAQUIN®, 1109 patients with cUTI and AP were enrolled in a randomized, double-blind, multicenter clinical trial conducted in the US from November 2004 to April 2006 comparing LEVAQUIN® 750 mg IV or orally once daily for 5 days (546 patients) with ciprofloxacin 400 mg IV or 500 mg orally twice daily for 10 days (563 patients). Patients with AP complicated by underlying renal diseases or conditions such as complete obstruction, surgery, transplantation, concurrent infection or congenital malformation were excluded. Efficacy was measured by bacteriologic eradication of the baseline organism(s) at the post-therapy visit in patients with a pathogen identified at baseline.

The bacteriologic cure rates overall for LEVAQUIN® minus ciprofloxacin (95% CI [-12.98, 8.98] for LEVAQUIN® minus ciprofloxacin). The overall eradication rates for pathogens of interest are presented in Table 19.
Table 20: Bacteriologic Eradication at Test-Of-Cure

<table>
<thead>
<tr>
<th>Pathogen Microbiologic Eradication Rate (n/N)</th>
<th>%</th>
<th>n/N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli*</td>
<td>155/172</td>
<td>90%</td>
<td>125/152</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>20/23</td>
<td>87.5</td>
<td>24/28</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>12/12</td>
<td>100%</td>
<td>9/9</td>
</tr>
</tbody>
</table>

* The predominant organism isolated from patients with AP was E. coli 91% (63/69) eradication in AP and 89% (92/103) in patients with UTI.

14.8 Complicated Urinary Tract Infections and Acute Pyelonephritis: 10-day Treatment Regimen

To evaluate the safety and efficacy of the 250 mg dose, 10 days regimen of LEVAQUIN®- 567 patients with uncomplicated UTI, mild-to-moderate cUTI, and mild-to-moderate AP were enrolled in a randomized, double-blind, multicenter clinical trial conducted in the US from June 1993 to January 1995 comparing LEVAQUIN®- 250 mg orally once for 10 days (285 patients) with ciprofloxacin 500 mg orally twice daily for 10 days (282 patients). Patients with a resistant pathogen, recurrent UTI, women over age 55 years, and with an indwelling catheter were initially excluded, prior to protocol amendment which took place after 30% of enrollment. Microbiological efficacy was measured by bacteriologic eradication of the baseline organism(s) at 1-2 days posttherapy in patients with a pathogen identified at baseline.

The bacteriologic cure rates overall for LEVAQUIN® and control at the test-of-cure (TOC) visit for the group of all patients with a documented pathogen at baseline (modified intent to treat or miITT) and the group of patients in the miITT population who closely followed the protocol (Microbiologically Evaluable) are summarized in Table 22.

Table 21: Microbiological Eradication Rates for Individual Pathogens Recovered From Patients Randomized to LEVAQUIN® 750 mg QD for 5 Days Treatment

<table>
<thead>
<tr>
<th>Pathogen Microbiologic Eradication Rate (n/N)</th>
<th>%</th>
<th>n/N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli*</td>
<td>155/172</td>
<td>90%</td>
<td>125/152</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>20/23</td>
<td>87.5</td>
<td>24/28</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>12/12</td>
<td>100%</td>
<td>9/9</td>
</tr>
</tbody>
</table>

* The predominant organism isolated from patients with AP was E. coli 91% (63/69) eradication in AP and 89% (92/103) in patients with UTI.

14.9 Inhalational Anthrax (Post-Exposure)

The effectiveness of LEVAQUIN® for this indication is based on plasma concentrations achieved in humans, a surrogate endpoint reasonably likely to predict clinical benefit. LEVAQUIN® has not been tested in humans for the post-exposure prevention of inhalation anthrax. The mean plasma concentrations of LEVAQUIN® associated with a statistically significant improvement in survival over placebo in the rhesus monkey model of inhalational anthrax were reached or exceeded in adult and pediatric patients receiving the recommended oral and intravenous dosage regimens [see Indications and Usage (1.12); Dosage and Administration (2.1, 2.2)].

Levofoxacin pharmacokinetics have been evaluated in adult and pediatric patients. The mean (± SD) steady state peak plasma concentration in human adults receiving 500 mg orally or intravenously once daily is 5.7 ± 1.4 and 6.4 ± 0.8 mcg/mL, respectively; and the corresponding total plasma exposure (AUC_{0-24}) is 47.5 ± 6.7 and 54.6 ± 11.1 mcg.h/mL, respectively. The predicted steady-state pharmacokinetic parameters in pediatric patients ranging in age from 6 months to 17 years receiving 8 mg/kg orally every 12 hours (not to exceed 250 mg per dose) were calculated to be comparable to those observed in adults receiving 500 mg orally once daily [see Clinical Pharmacology (12.3)].

In adults, the safety of LEVAQUIN® for treatment durations of up to 28 days is well characterized. However, information pertaining to extended use of 500 mg up to 60 days is limited. Prolonged LEVAQUIN® therapy in adults should only be used when the benefit outweighs the risk.

In pediatric patients, the safety of levofoxacin for treatment durations of more than 14 days has not been studied. An increased incidence of musculoskeletal adverse events (arthralgia, arthritis, tendopathy, gait abnormality) compared to controls has been observed in clinical studies with treatment duration of up to 14 days. Long-term safety data, including effects on cartilage, following the administration of levofoxacin to pediatric patients is limited [see Warnings and Precautions (5.3), Use in Specific Populations (8.4)].

A placebo-controlled animal study in rhesus monkeys exposed to an inhaled mean dose of 49 LD_{50} (2.7 x 10^{10}) spores (range 17 – 118 LD_{50} of B. anthracis Ames strain) was conducted. The minimal inhibitory concentration (MIC) of levofoxacin for the anthrax strain used in this study was 0.125 mcg/mL. In the animals studied, mean plasma concentrations of levofoxacin achieved at expected T_{max} (1 hour post-dose) following oral dosing to steady state ranged from 2.79 to 4.97 mcg/mL. Steady state trough concentrations at 24 hours post-dose ranged from 0.107 to 0.164 mcg/mL. Mean (SD) steady state AUC_{24} was 33.4 ± 3.2 mcg.h/mL (range 30.4 to 36.0 mcg.h/mL). Mortality due to anthrax for animals that received a 30 day regimen of oral LEVAQUIN® beginning 24 hours post-exposure was significantly lower (11/10), compared to the placebo group (8/10) [P=0.0011, 2-sided Fisher’s Exact Test]. The one levofoxacin treated animal that died of anthrax did so following the 30-day drug administration period.

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 LEVAQUIN® Tablets

LEVAQUIN® Tablets are supplied as 250, 500, and 750 mg capsule-shaped, coated tablets. LEVAQUIN® Tablets are packaged in bottles and in unit-dose blister strips in the following configurations:
- 250 mg tablets are terra cotta pink and are imprinted: “LEVAQUIN” on one side and “250” on the other side.
- 500 mg tablets are peach and are imprinted: “LEVAQUIN” on one side and “500” on the other side.
- 750 mg tablets are white and are imprinted “LEVAQUIN” on one side and “750” on the other side.
- Each bottle contains 480 mL of the 25 mg/mL levofloxacin oral solution
- Each bottle contains 480 mL of the 25 mg/mL levofloxacin oral solution

LEVAQUIN® Tablets should be stored at 15° to 30°C (59° to 86°F) in well-closed containers.

LEVAQUIN® Tablets are manufactured for PriCara, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc., Raritan, NJ 08869 by Janssen Ortho LLC, Gurabo, Puerto Rico 00778.

16.2 LEVAQUIN® Oral Solution

LEVAQUIN® Oral Solution is supplied in a 16 oz. multi-use bottle (NDC 50458-170-01). Each bottle contains 480 mL of the 25 mg/mL levofloxacin oral solution

LEVAQUIN® Oral Solution should be stored at 25°C (77°F); excursions permitted to 15°-30°C (59° to 86°F) (refer to USP controlled room temperature).


16.3 LEVAQUIN® Injection, Single-Use Vials

LEVAQUIN® Injection is supplied in single-use vials. Each vial contains a concentrated solution with the equivalent of 500 mg of levofloxacin in 20 mL and 750 mg of levofloxacin in 30 mL vials.
- 25 mg/mL, 20 mL vials (NDC 50458-164-20)
- 25 mg/mL, 30 mL vials (NDC 50458-165-30)

LEVAQUIN® Injection in Single-Use Vials should be stored at controlled room temperature and protected from light.

LEVAQUIN® (levofloxacin) Injection, for Intravenous Use

16.4 LEVAQUIN® Injection Pre-Mixed Solution, Single-Use in Flexible Container

LEVAQUIN® (levofloxacin in 5% dextrose) Injection is supplied as a single-use, premixed solution in flexible containers. Each bag contains a dilute solution with the equivalent of 250, 500, or 750 mg of levofloxacin, respectively, in 5% Dextrose (USP).

- 5 mg/mL (250 mg), 100 mL flexible container, 50 mL fill (NDC 50458-167-01)
- 5 mg/mL (500 mg), 100 mL flexible container, 100 mL fill (NDC 50458-168-01)
- 5 mg/mL (750 mg), 150 mL flexible container, 150 mL fill (NDC 50458-168-01)

LEVAQUIN® Injection Premix in Flexible Containers should be stored at or below 25°C (77°F); however, brief exposure up to 40°C (104°F) does not adversely affect the product. Avoid excessive heat and protect from freezing and light.

LEVAQUIN® Injection Premix in Flexible Containers is manufactured for Ortho-McNeil, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc., Raritan, NJ 08869 by Hospira, Inc., Lake Forest, IL 60045.

17 PATIENT COUNSELING INFORMATION

See FDA-Approved Medication Guide (17.5)

17.1 Antibacterial Resistance

Antibacterial drugs including LEVAQUIN® should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When LEVAQUIN® is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by LEVAQUIN® or other antibacterial drugs in the future.

17.2 Administration with Food, Fluids, and Concomitant Medications

Patients should be informed that LEVAQUIN® Tablets may be taken with or without food. LEVAQUIN® Oral Solution should be taken 1 hour before or 2 hours after eating. The tablet and oral solution should be taken at the same time each day.

Patients should drink fluids liberally while taking LEVAQUIN® to avoid formation of a highly concentrated urine and crystal formation in the urine.

Antacids containing magnesium, or aluminum, as well as sucralfat, metal cations such as iron, and multivitamin preparations with zinc or didanosine should be taken at least two hours before or two hours after oral LEVAQUIN® administration.

17.3 Serious and Potentially Serious Adverse Reactions

Patients should be informed of the following serious adverse reactions that have been associated with LEVAQUIN® or other fluoroquinolones use:

- **Tendon Disorders**: Patients should contact their healthcare provider if they experience pain, swelling, or inflammation of a tendon, or weakness or inability to use one of their joints; rest and refrain from exercise; and discontinued LEVAQUIN® treatment. The risk of severe tendon disorders with fluoroquinolones is higher in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart, or lung transplants.

- **Hypersensitivity Reactions**: Patients should be informed that LEVAQUIN® can cause hypersensitivity reactions, even following the first dose. Patients should discontinue the drug at the first sign of a skin rash, hives or other skin reactions, a rapid heartbeat, difficulty in swallowing or breathing, any swelling suggesting angioedema (e.g., swelling of the lips, tongue, face, tightness of the throat, hoarseness), or other symptoms of an allergic reaction.

- **Hepatotoxicity**: Severe hepatotoxicity (including acute hepatitis and fatal events) has been reported in patients taking LEVAQUIN®. Patients should inform their physician and be instructed to discontinue LEVAQUIN® treatment immediately if they experience any signs or symptoms of liver injury including: loss of appetite, nausea, vomiting, fever, weakness, tiredness, right upper quadrant tenderness, itching, yellowing of the skin and eyes, light colored bowel movements or dark colored urine.

- **Convulsions**: Convulsions have been reported in patients taking fluoroquinolones, including LEVAQUIN®. Patients should notify their physician before taking this drug if they have a history of convulsions.

- **Neurologic Adverse Effects (e.g., dizziness, lightheadedness)**: Patients should know how they react to LEVAQUIN® before they operate an automobile or machinery or engage in other activities requiring mental alertness and coordination.

- **Diarrhea**: Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

- **Peripheral Neuropathy**: If symptoms of peripheral neuropathy including pain, burning, tingling, numbness, and/or weakness develop, patients should discontinue treatment and contact their physician.

- **Prolongation of the QT Interval**: Patients should inform their physician of any personal or family history of QT prolongation or proarrhythmic conditions such as hypokalemia, bradycardia, or recent myocardial ischemia; if they are taking any Class IA (quinidine, procainamide), or Class III (amiodarone, sotalol) antiarrhythmic agents. Patients should notify their physicians if they have any symptoms of prolongation of the QT interval, including prolonged heart palpitations or a loss of consciousness.

17.4 Drug Interactions with Insulin, Oral Hypoglycemic Agents, and Warfarin

Patients should be informed that if they are diabetic and are being treated with insulin or an oral hypoglycemic agent and a hypoglycemic reaction occurs, they should discontinue LEVAQUIN® and consult a physician.

Patients should be informed that concurrent administration of warfarin and LEVAQUIN® has been associated with increases of the International Normalized Ratio (INR) or prothrombin time and clinical episodes of bleeding. Patients should notify their physician if they are taking warfarin, be monitored for evidence of bleeding, and also have their anticoagulation tests closely monitored while taking warfarin concomitantly.

Manufactured by:

- Janssen Ortho LLC, Curabo, Puerto Rico 00778 (for the Tablets).
- Janssen Pharmaceutica N.V., Beerse, Belgium (for the Oral Solution and Injection, Single-Use Vials).
- Hospira, Inc., Lake Forest, IL 60045 (for the Injection Pre-Mixed Solution Single-Use in Flexible Container).

Manufactured for:

- PriCara, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc., Raritan, NJ 08869 (for the Tablets and Oral Solution)

© Ortho-McNeil-Janssen Pharmaceuticals, Inc.


17.5 FDA-Approved Medication Guide

**MEDICATION GUIDE

LEVAQUIN® [leave ah kwln] (levofloxacin)

250 mg Tablets, 500 mg Tablets, and 750 mg Tablets

And

LEVAQUIN® (levofloxacin) Oral Solution, 25 mg/mL

And

LEVAQUIN® (levofloxacin) Injection, for Intravenous Use

And

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

Read the Medication Guide that comes with LEVAQUIN® before you start taking it 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® belongs to a class of antibiotics called fluoroquinolones. LEVAQUIN® can cause side effects that may be serious or even cause death. If you get any of the following serious side effects, get medical help right away. Talk with your healthcare provider about whether you should continue to take LEVAQUIN®.

- **Tendon rupture or swelling of the tendon (tendinitis)**:
  - Tendons are tough cords of tissue that connect muscles to bones.
  - Pain, swelling, tears, and inflammation of tendons including the back of the ankle (Achilles), shoulder, hand, or other tendon sites can happen in people of all ages who take fluoroquinolone antibiotics, including LEVAQUIN®. The risk of getting tendon problems is higher if you:
    - are over 60 years of age
    - are taking steroids (corticosteroids)
    - have had a kidney, heart or lung transplant.
LEVAQUIN® (levofloxacin)

- Swelling of the tendon (tendinitis) and tendon rupture (breakage) have also happened in patients who take fluoroquinolones who do not have the above risk factors.
- Other reasons for tendon ruptures can include:
  - physical activity or exercise
  - kidney failure
  - 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 patients have finished taking their fluoroquinolone.
- Get medical help right away if you get any of the following signs or symptoms of a tendon rupture:
  - hear or feel a snap or pop in a tendon area
  - bruising right after an injury in a tendon area
  - unable to move the affected area or bear weight
- Tendon pain, swelling or inflammation. Stop taking LEVAQUIN®
- A tendinitis or tendon rupture has happened up to several months after patients have finished taking their fluoroquinolone.
- Other reasons for tendon ruptures can include:
  - 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. See "What are the possible side effects of LEVAQUIN®?" if you are not sure if any of your medicines are listed above.
  - a blood thinner (warfarin, Coumadin, Jantoven). Aortic valve replacement has happened up to several months after patients have finished taking their fluoroquinolone.
  - a tricyclic antidepressant
  - a water pill (diuretic)
  - a steroid medicine. Corticosteroids taken by mouth or by injection may increase the chance of tendon injury. See "What are the possible side effects of LEVAQUIN®?"
  - theophylline (Theo-24®, Elixophyllin®, Theochron®, Uniphyl®, Theolair®)
  - certain medicines may keep LEVAQUIN® from working correctly. Take LEVAQUIN® Tablets or Oral Solution either 2 hours before or 2 hours after taking these products:
    - an antacid, multivitamin, or other product that has magnesium, aluminum, iron, or zinc.
    - sucralfate (Carafate®)
    - didanosine (Videx®, Videx® EC)

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, herbal and dietary supplements. LEVAQUIN® and other medicines can affect each other causing side effects. Especially tell your healthcare provider if you take:

- an oral anti-diabetes medicine or insulin
- a blood thinner (warfarin, Coumadin, Jantoven)
- a medicine to control your heart rate or rhythm (antiarrhythmics). See "What are the possible side effects of LEVAQUIN®?"
- an anti-psychotic medicine
- a tricyclic antidepressant
- a water pill (diuretic)
- a steroid medicine. Corticosteroids taken by mouth or by injection may increase the chance of tendon injury. See "What are the possible side effects of LEVAQUIN®?"
- theophylline (Theo-24®, Elixophyllin®, Theochron®, Uniphyl®, Theolair®)
- certain medicines may keep LEVAQUIN® from working correctly. Take LEVAQUIN® Tablets or Oral Solution either 2 hours before or 2 hours after taking these products:
  - an antacid, multivitamin, or other product that has magnesium, aluminum, iron, or zinc.
  - sucralfate (Carafate®)
  - didanosine (Videx®, Videx® EC)

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 prescribed by your healthcare provider.
- Take LEVAQUIN® at about the same time each day.
- Drink plenty of fluids while taking 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 one dose in one day.
- LEVAQUIN® for Injection is given to you by intravenous (I.V.) infusion into your vein, slowly, over 60 or 90 minutes, as prescribed by your healthcare provider. See "What are the possible side effects of LEVAQUIN®?"

LEVAQUIN® (levofloxacin)

- 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 a history of seizures
- have bone and joint problems
- have kidney problems. You may need a lower dose of LEVAQUIN® if your kidneys do not work well.
- have liver problems
- have rheumatoid arthritis (RA) or other history of joint problems
- are pregnant or planning to become pregnant. It is not known if LEVAQUIN® will harm your unborn child.
- are breast-feeding or planning to breast-feed. LEVAQUIN® is thought to pass into breast milk. You and your healthcare provider should decide whether you will take LEVAQUIN® or breast-feed.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, herbal and dietary supplements. LEVAQUIN® and other medicines can affect each other causing side effects. Especially tell your healthcare provider if you take:

- 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. See "What are the possible side effects of LEVAQUIN®?"
- an oral anti-diabetes medicine or insulin
- a blood thinner (warfarin, Coumadin, Jantoven)
- a medicine to control your heart rate or rhythm (antiarrhythmics). See "What are the possible side effects of LEVAQUIN®?"
- an anti-psychotic medicine
- a tricyclic antidepressant
- a water pill (diuretic)
- a steroid medicine. Corticosteroids taken by mouth or by injection may increase the chance of tendon injury. See "What are the possible side effects of LEVAQUIN®?"
- theophylline (Theo-24®, Elixophyllin®, Theochron®, Uniphyl®, Theolair®)
- certain medicines may keep LEVAQUIN® from working correctly. Take LEVAQUIN® Tablets or Oral Solution either 2 hours before or 2 hours after taking these products:
  - an antacid, multivitamin, or other product that has magnesium, aluminum, iron, or zinc.
  - sucralfate (Carafate®)
  - didanosine (Videx®, Videx® EC)

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 prescribed by your healthcare provider.
- Take LEVAQUIN® at about the same time each day.
- Drink plenty of fluids while taking 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 one dose in one day.
- LEVAQUIN® for Injection is given to you by intravenous (I.V.) infusion into your vein, slowly, over 60 or 90 minutes, as prescribed by your healthcare provider. See "What are the possible side effects of LEVAQUIN®?"

LEVAQUIN® (levofloxacin)

- 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 a history of seizures
- have bone and joint problems
- have kidney problems. You may need a lower dose of LEVAQUIN® if your kidneys do not work well.
- have liver problems
- have rheumatoid arthritis (RA) or other history of joint problems
- are pregnant or planning to become pregnant. It is not known if LEVAQUIN® will harm your unborn child.
- are breast-feeding or planning to breast-feed. LEVAQUIN® is thought to pass into breast milk. You and your healthcare provider should decide whether you will take LEVAQUIN® or breast-feed.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, herbal and dietary supplements. LEVAQUIN® and other medicines can affect each other causing side effects. Especially tell your healthcare provider if you take:

- 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. See "What are the possible side effects of LEVAQUIN®?"
- an oral anti-diabetes medicine or insulin
- a blood thinner (warfarin, Coumadin, Jantoven)
- a medicine to control your heart rate or rhythm (antiarrhythmics). See "What are the possible side effects of LEVAQUIN®?"
- an anti-psychotic medicine
- a tricyclic antidepressant
- a water pill (diuretic)
- a steroid medicine. Corticosteroids taken by mouth or by injection may increase the chance of tendon injury. See "What are the possible side effects of LEVAQUIN®?"
- theophylline (Theo-24®, Elixophyllin®, Theochron®, Uniphyl®, Theolair®)
- certain medicines may keep LEVAQUIN® from working correctly. Take LEVAQUIN® Tablets or Oral Solution either 2 hours before or 2 hours after taking these products:
  - an antacid, multivitamin, or other product that has magnesium, aluminum, iron, or zinc.
  - sucralfate (Carafate®)
  - didanosine (Videx®, Videx® EC)

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 prescribed by your healthcare provider.
- Take LEVAQUIN® at about the same time each day.
- Drink plenty of fluids while taking 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 one dose in one day.
- LEVAQUIN® for Injection is given to you by intravenous (I.V.) infusion into your vein, slowly, over 60 or 90 minutes, as prescribed by your healthcare provider. See "What are the possible side effects of LEVAQUIN®?"
If you have been prescribed LEVAQUIN® after being exposed to anthrax:
- LEVAQUIN® has been approved to lessen the chance of getting anthrax disease or worsening of the disease after you are exposed to the anthrax bacteria germ.
- Take LEVAQUIN® exactly as prescribed by your healthcare provider. Do not stop taking LEVAQUIN® without talking with your healthcare provider. If you stop taking LEVAQUIN® too soon, it may not keep you from getting the anthrax disease.
- Side effects may happen while you are taking LEVAQUIN®. When taking LEVAQUIN® to prevent anthrax infection, you and your healthcare provider should talk about whether the risks of stopping your medicine too soon are more important than the risks of side effects with LEVAQUIN®. It is not known if it is safe to use LEVAQUIN® for more than 28 days in adults and for more than 14 days in children 6 months of age and older.
- If you are pregnant, or plan to become pregnant while taking LEVAQUIN®, you and your healthcare provider should decide whether the benefits of taking LEVAQUIN® for anthrax are more important than the risks.

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 taking 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 side effects that may be serious or even cause death. See “What is the most important information I should know about LEVAQUIN®?”

Other serious side effects of LEVAQUIN® include:
- **Liver damage (hepatotoxicity):** Liver damage (hepatotoxicity) can happen in people who take LEVAQUIN®. Call your healthcare provider right away if you have unexplained symptoms such as:
  - nausea or vomiting,
  - stomach pain,
  - fever,
  - weakness,
  - abdominal pain or tenderness,
  - itching,
  - unusual tiredness,
  - loss of appetite,
  - light colored bowel movements,
  - dark colored urine or yellowing of your skin or the whites of your eyes.

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

- **Serious allergic reactions.** Allergic reactions can happen in people taking fluoroquinolones, including LEVAQUIN®, even after only one dose. Stop taking LEVAQUIN® and get emergency medical help right away if you get any of the following symptoms of a severe allergic reaction:
  - hives
  - trouble breathing or swallowing
  - swelling of the lips, tongue, face
  - throat tightness, hoarseness
  - rapid heartbeat
  - faint
  - Yellowing of the skin or eyes. Stop taking LEVAQUIN® and tell your healthcare provider right away if you get 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).

- **Skin rash**
Skin rash may happen in people taking LEVAQUIN®, even after only one 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®.

- **Intestine infection (Pseudomembranous colitis)**
Pseudomembranous colitis can happen with most 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 possible nerve damage (Peripheral Neuropathy)**
Damage to the nerves in arms, hands, legs, or feet can happen in people taking fluoroquinolones, including LEVAQUIN®. 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:
  - pain
  - burning
  - tingling
  - numbness
  - weakness

LEVAQUIN® may need to be stopped to prevent permanent nerve damage.
LEVAQUIN® (levofloxacin)

- **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:
  - who are elderly
  - with a family history of prolonged QT interval
  - with low blood potassium (hypokalemia)
  - who take certain medicines to control heart rhythm (antiarrhythmics)

- **Changes in blood sugar [low blood sugar (hypoglycemia) and high blood sugar (hyperglycemia)]**
  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 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®?”

- **Joint Problems**
  Increased chance of problems with joints and tissues around joints in children. Tell your child’s healthcare provider if your child has any joint problems during or after treatment with LEVAQUIN®.

The most common side effects of LEVAQUIN® include:
- dizziness
- headache
- constipation
- nausea
- diarrhea

In children 6 months and older who take LEVAQUIN® to prevent anthrax disease, vomiting is also common.

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

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® Film-Coated Tablets at 59°F to 86°F (15°C to 30°C). Keep the container closed tightly.

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 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.