**TEQUIN® (gatifloxacin) Tablets**

**TEQUIN® (gatifloxacin in 5% dextrose) Injection**

(Patient Information Included)

TEQUIN® is available as TEQUIN (gatifloxacin) Tablets for oral administration and TEQUIN (gatifloxacin injection and TEQUIN (gatifloxacin in 5% dextrose) injection for intravenous administration.

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

**DESCRIPTION**

TEQUIN contains gatifloxacin, a synthetic broad-spectrum 8-methoxyfluoroquinolone antibacterial agent for oral or intravenous administration. Chemically, gatifloxacin is (6S)-1-cyclopropyl-6-fluoro-4-dihydro-7-(3-methyl-1-piperazinyl)-8-oxo-3-quinolinicarboxylic acid sesquihydrate.

The chemical structure is:

![Chemical Structure of Gatifloxacin](image)

Its empirical formula is C₁₉H₂₂FN₃O₄•1.5 H₂O and its molecular weight is 402.42. Gatifloxacin is a sesquihydric crystalline powder and is white to pale yellow in color. It exists as a racemate, with no net optical rotation. The solubility of the compound is pH dependent. The maximum aqueous solubility (40-60 mg/mL) occurs at a pH range of 2 to 5.

**TEQUIN Tablets**

TEQUIN Tablets are available as 200 mg and 400 mg white, film-coated tablets and contain the following inactive ingredients: hypromellose, magnesium stearate, methycellulose, microcrystalline cellulose, polyethylene glycol, polysorbate 80, simethicone, sodium starch glycolate, sorbic acid, and titanium dioxide.

**TEQUIN Injection for Intravenous Administration**

TEQUIN Injection is available in 40-mL (400 mg) single-use vials as a sterile, preservative-free, aqueous solution of gatifloxacin with pH ranging from 3.5 to 5. TEQUIN Injection (gatifloxacin in 5% dextrose) injection is also available in ready-to-use 100-mL (400 mg) and 200-mL (400 mg) flexible bags as a sterile, preservative-free, aqueous solution of gatifloxacin with pH ranging from 3.5 to 5. The appearance of the intravenous solution may range from light yellow to greenish-yellow in color. The color does not affect nor is it indicative of product stability.

The intravenous formulation contains dextrose, anhydrous, USP or dextrose, monohydrate, USP and Water for Injection, USP, and may contain hydrochloric acid and/or sodium hydroxide for pH adjustment.

**CLINICAL PHARMACOLOGY**

Gatifloxacin is administered as a racemate, with the disposition and antibacterial activity of the R- and S-enantiomers virtually identical.

**Absorption**

Gatifloxacin is well absorbed from the gastrointestinal tract after oral administration and can be given without regard to food. The absolute bioavailability of gatifloxacin tablets is 96%. Peak plasma concentrations of gatifloxacin usually occur 1-2 hours after oral dosing under fasted conditions.

**Distribution**

Serum protein binding of gatifloxacin is approximately 20% in volunteers and is concentration independent. Consistent with the low protein binding, concentrations of gatifloxacin in saliva were approximately equal to those in plasma (mean [range] saliva/plasma ratio was 0.88 [0.46-1.57]). The mean volume of distribution of gatifloxacin at steady-state (Vdss) ranged from 1.5 to 2.0 L/kg. Gatifloxacin is widely distributed throughout the body into many body tissues and fluids. Rapid distribution of gatifloxacin into tissues results in higher gatifloxacin concentrations in most target tissues than in serum (Table 3).

**Pharmacokinetics**

The mean (SD) pharmacokinetic parameters of gatifloxacin following oral administration to healthy subjects with bacterial infections and subjects with renal insufficiency are listed in Table 1. The mean (SD) pharmacokinetic parameters of gatifloxacin following intravenous administration to healthy subjects are listed in Table 2.

Gatifloxacin pharmacokinetics are linear and time-independent at doses ranging from 200 to 800 mg administered over a period of up to 14 days. Steady-state concentrations are achieved by the third daily oral or intravenous dose of gatifloxacin. The mean steady-state peak and trough plasma concentrations attained following a dosing regimen of 400 mg once daily are approximately 4.2 mcg/mL and 0.4 mcg/mL, respectively, for oral administration and 4.6 mcg/mL and 0.4 mcg/mL, respectively, for intravenous administration. The tablets and oral suspension are bioequivalent and are anticipated to result in similar steady-state exposures.

**Adverse Reactions**

Common adverse reactions associated with the use of gatifloxacin tablets are nausea, diarrhea, anorexia, and headache. Rare, but serious, adverse events include respiratory tract infections, Stevens-Johnson syndrome, and cutaneous reactions, including photosensitivity reactions.

**Table 1: Gatifloxacin Pharmacokinetic Parameters — Oral Administration**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cmax (mcg/mL)</th>
<th>Tmax (h)</th>
<th>AUC∞(mcg*h/mL)</th>
<th>T1/2 (h)</th>
<th>Cl/F (mL/min)</th>
<th>C18 (mL/min)</th>
<th>UR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 mg, Tablet — Healthy Volunteers</td>
<td>2.0 ± 0.4</td>
<td>1.00 (0.50, 2.50)</td>
<td>14.2 ± 0.4</td>
<td>—</td>
<td>241 ± 40</td>
<td>—</td>
<td>73.8 ± 10.9</td>
</tr>
<tr>
<td>400 mg, Tablet — Healthy Volunteers</td>
<td>3.8 ± 1.0</td>
<td>1.00 (0.50, 6.00)</td>
<td>33.0 ± 6.2</td>
<td>7.8 ± 1.3</td>
<td>210 ± 44</td>
<td>151 ± 46</td>
<td>72.4 ± 18.1</td>
</tr>
<tr>
<td>400 mg, Oral Suspension — Healthy Volunteers</td>
<td>4.2 ± 1.3</td>
<td>1.50 (0.40, 4.00)</td>
<td>34.4 ± 0.7</td>
<td>7.1 ± 0.6</td>
<td>199 ± 31</td>
<td>159 ± 34</td>
<td>80.2 ± 12.1</td>
</tr>
<tr>
<td>400 mg, Tablet — Patients with Infection</td>
<td>3.2 ± 0.6</td>
<td>1.25 (0.50, 4.00)</td>
<td>30.0 ± 8.8</td>
<td>8.5 ± 1.1</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>400 mg, Tablet — Subjects with Renal Insufficiency, Single Dose</td>
<td>4.2 ± 1.9</td>
<td>—</td>
<td>51.3 ± 20.4</td>
<td>—</td>
<td>147 ± 48</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

**Table 2: Gatifloxacin Mean ± SD Pharmacokinetic Parameters — Intravenous Administration**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cmax (mcg/mL)</th>
<th>Tmax (h)</th>
<th>AUC∞(mcg*h/mL)</th>
<th>T1/2 (h)</th>
<th>Vdss (L/kg)</th>
<th>CI (mL/min)</th>
<th>C18 (mL/min)</th>
<th>UR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 mg — Healthy Volunteers</td>
<td>2.2 ± 0.3</td>
<td>1.00 (0.67, 1.50)</td>
<td>15.9 ± 2.6</td>
<td>11.1 ± 4.1</td>
<td>1.9 ± 0.1</td>
<td>214 ± 36</td>
<td>155 ± 32</td>
<td>71.7 ± 6.8</td>
</tr>
<tr>
<td>400 mg — Healthy Volunteers</td>
<td>2.4 ± 0.4</td>
<td>1.00 (0.67, 1.00)</td>
<td>16.8 ± 3.6</td>
<td>12.3 ± 4.6</td>
<td>2.0 ± 0.3</td>
<td>207 ± 44</td>
<td>155 ± 55</td>
<td>72.4 ± 16.4</td>
</tr>
</tbody>
</table>

**Figure 1: Mean Plasma Concentration-Time Profiles of Gatifloxacin Following Intravenous (IV) and Oral (PO) Tablet Administration of a Single 400 mg Dose to Healthy Subjects.**

**Table 3: Gatifloxacin Tissue — Fluid/ Serum Ratio (Range)**

<table>
<thead>
<tr>
<th>Fluid or Tissue</th>
<th>Tissue/Fluid</th>
<th>Serum Ratio (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>26.5 (10.9-61.1)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Bronchial mucosa</td>
<td>1.65 (1.2-2.22)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Lung epithelial lining fluid</td>
<td>1.67 (0.8-4.46)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Lung parenchyma</td>
<td>4.09 (0.50-9.22)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Sinus mucosa</td>
<td>1.78 (1.17-2.49)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Sputum (Multiple Dose)</td>
<td>1.28 (0.49-2.38)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Skin</td>
<td>1.00 (0.50-1.47)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Reproductive</td>
<td>1.07 (0.86-1.32)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Seminal fluid</td>
<td>1.01 (0.81-1.21)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Vagina</td>
<td>1.22 (0.57-1.63)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Cervix</td>
<td>1.45 (0.56-2.64)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
</tbody>
</table>

*Mean of individual ratios collected over 24 hours following single (100, 150, 200, 300, or 400 mg) or multiple (150 or 200 mg BID) doses of gatifloxacin except for skin blister fluid, where mean AUC ratio is presented.*

*Note: All the above values are presented as median (minimum, maximum).
Metabolism
Gatifloxacin undergoes limited biotransformation in humans with less than 1% of the dose excreted in the urine as ethylendiamine and methylendiamine metabolites.
In vivo studies with human P450 isozymes (CYP) indicate that gatifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2, suggesting that gatifloxacin is unlikely to alter the pharmacokinetics of drugs metabolized by these enzymes (e.g., midazolam, cyclosporine, warfarin, theophylline).
In in vitro studies with human P450 enzymes, gatifloxacin had no inhibitory effect on any of the isoenzymes tested (CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4). Therefore, gatifloxacin is unlikely to alter the metabolic elimination of itself or other coadministered drugs.
Excretion
Gatifloxacin is excreted as unchanged drug primarily by the kidney. More than 70% of an administered TEQUIN (gatifloxacin) dose was recovered as unchanged drug in the urine within 48 hours following oral administration. Gatifloxacin protein binding in serum is 27–30%. Less than 5% of gatifloxacin is recovered in the feces. Crystalluria has occurred in dogs and has not been recovered in the urine as two metabolites. Crystals of gatifloxacin have not been observed in the urine of normal healthy volunteers. In patients with impaired renal function, gatifloxacin is excreted primarily by glomerular filtration and/or tubular secretion. Gatifloxacin may also undergo minimal biliary and/or intestinal elimination, since 5% of dose was recovered in the feces as unchanged drug. This finding is supported by the 5-fold higher concentration of gatifloxacin in the bile compared to the plasma (mean bile/ plasma ratio of 3.3–4.1).
Special Populations
Patients with Bacterial infections
The pharmacokinetics of gatifloxacin in pre- and post-dose ECGs, the mean change in the post-dose QTc interval was less than 60 milliseconds from baseline and there was no cross-reactivity between gatifloxacin and the mentioned classes of antibiotics.
### Microbiological Testing

**Susceptibility Tests**

**Dilution Techniques:**
Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. One such standard method is the broth dilution technique using HTM.1

**Zone Diameter Interpretation:**
- **Zone Diameter (mm):**
  - S: 17 - 19
  - I: 15 - 17
  - R: ≤14

**MIC (mcg/mL):**
- **Zone Diameter (mm):**
  - S: 17 - 19
  - I: 15 - 17
  - R: ≤14

**NOTE:** These zone diameter standards only apply to tests performed using Mueller-Hinton agar supplemented with 5% sheep blood incubated in 5% CO₂.

Indications and Usage:
- **Acute bacterial exacerbation of chronic bronchitis due to Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis:**
- **Acute sinusitis due to Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis:**
- **Community-acquired pneumonia due to Streptococcus pneumoniae:**

**Microorganisms:**
- **Staphylococcus aureus**
- **Escherichia coli**
- **Pseudomonas aeruginosa**
- **Enterococcus faecalis**
- **Neisseria gonorrhoeae**

**MIC Range (mcg/mL):**
- **MIC < 0.12:** S
- **MIC < 1.0:** I
- **MIC ≥ 4.0:** R

### Other Information

- **Ampicillin/sulbactam (2:1 reducing agent):**
- **Antisense oligonucleotides:**
- **Bacterial transduction:**
- **Bacteriophage:**
- **Bacterial chemolysin:**

### References

1. HTM: Hospital Testing Method.
2. MIC: Minimum Inhibitory Concentration.
performed. Gatifloxacin should be used with caution when given concurrently with these drugs, as well as in patients with ongoing prearthritic conditions, such as clinically significant bradycardia or acute myocardial ischemia.

- Prolactin levels and free T4 levels may increase following administration of gatifloxacin, which may result in clinically significant changes in thyroid function and breast enlargement in women. However, information concerning the effects of gatifloxacin on TSH levels is limited.

- The safety and effectiveness of gatifloxacin in pediatric patients less than 18 years of age have not been established. Gatifloxacin is excreted in the breast milk of rats. It is not known whether gatifloxacin is excreted in human breast milk.
In patients who were treated with either intravenous gatifloxacin or intravenous with followed by oral therapy, the incidence of adverse events was similar to those who received oral therapy alone. Local injection site reactions (redness at injection site) were noted in 5% of patients.

Additional drug-related events (possibly, definitely related) considered clinically relevant that occurred in 0.1% to <3% of patients receiving gatifloxacin in single- and multiple-dose clinical trials are as follows: abdominal pain, abdominal distention, abnormal vision, anaphylactic reaction, atrial fibrillation, atrial flutter, atrial tachycardia, azotemia, bruising, cellulitis, chest pain, chills, facial edema, fever, hypovolemia, hypertension, hyperthermia, hypotension, interstitial nephritis, leukopenia, lower urinary tract infection, methemoglobinemia, myalgia, muscle cramps, myopathy, nausea, phlebitis, pruritus, psychiatric disorder, pyelonephritis, renal failure, respiratory distress syndrome, sepsis, seizures, urticaria, vomiting, worsening of asthma.

Clinical Laboratory Changes

Laboratory changes clinically relevant in laboratory parameters, without regard to drug relationship, occurred in fewer than 1% of TEQUIN-treated patients. These included: hyperglycemia, increased AST or ALT levels, alkaline phosphatase, bilirubin, serum amylase, and electrolyte abnormalities. It is not known whether these abnormalities were caused by the drug or the underlying condition being treated.

Postmarketing Adverse Event Reports

The following events have been reported during postapproval use of TEQUIN. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Abnormal renal function from acute allergic reaction including anaphylactic reaction and anorexia neonatae, hepatitis, hypotension, increased International Normalized Ratio (INR)/prothrombin time, pancreatitis, severe hyperglycemia (including hyperosmolar nonketotic hyperglycemia), rash, rhabdomyolysis, Stevens-Johnson syndrome, syncope, tinnitus, urticaria, vasculitis, vomiting.

OVERDOSAGE

In the event of acute oral overdose, the stomach should be emptied by inducing vomiting or by gastric lavage. The patient should be carefully observed (including ECG monitoring) and given symptomatic and supportive treatment. Adequate hydration should be maintained. Gatifloxacin is not efficiently removed from the body by hemodialysis (approximately 11% recovered over 4 hours) or by chronic ambulatory peritoneal dialysis (CAPD) (approximately 11% recovered over 8 days).

DOSAGE AND ADMINISTRATION

General Information

TEQUIN Tablets or TEQUIN Injection is described in Table 4. Doses of TEQUIN are administered once every 24 hours. These recommendations apply to all patients with a normal renal function.

The recommended dosage for TEQUIN Tablets or TEQUIN Injection is described in Table 4. Doses of TEQUIN are administered once every 24 hours. These recommendations apply to all patients with a normal renal function.

In patients with impaired renal function, the clearance of TEQUIN (gatifloxacin) is necessary in patients with moderate hepatic impairment (Child-Pugh Class B). There are no data in patients with severe hepatic impairment (Child-Pugh Class C) (see CLINICAL PHARMACOLOGY).

Intravenous Administration

Preparation of Gatifloxacin for Intravenous Administration

TEQUIN Injection is supplied in single-use 40-mL vials (10 mg/mL) containing a concentrated solution of gatifloxacin in 5% dextrose (400 mg of gatifloxacin) [see HOW SUPPLIED]. DILUTION OF SINGLE-USE VIALS MUST BE FURTHER DILUTED WITH APPROPRIATE SOLUTION PRIOR TO INTRAVENOUS ADMINISTRATION. The concentration of the resulting diluted solution should be 2 mg/mL prior to administration.

This intravenous drug product should be inspected visually for particulate matter prior to dilution and administration. If this product is visibly discolored or if the vial becomes warm, do not use. A bacteriostatic agent is present in this product, aseptic technique must be used in preparation of the final dose. Since the vials are for single-use only, any unused portion remaining in the vial should be discarded.

Since only limited data are available on the compatibility of gatifloxacin intravenous injection with other intravenous solutions, diluent or other medications should not be added to TEQUIN injection in single-use vials or infused simultaneously through the same intravenous line. If the same intravenous line is used for sequential infusion of different drugs, the line should be flushed before and after infusion of TEQUIN injection with an infusion solution compatible with TEQUIN injection and with any other drug(s) administered via this common line.

Intravenous doses for the use of TEQUIN (gatifloxacin in 5% dextrose) injection premix in flexible containers:

To open: 1. Tear outer wrap at the notch and remove solution container. 2. Check the container for intactness. 3. Insert piercing pin of administration set or tongue depressor into the inner bag firm. If leaks are found, or if the seal is not intact, discard the solution, as the sterility may be compromised.

Use only if solution is clear and light yellow to greenish-yellow in color.

Intravenous Premix in Flexible Containers

Storage

Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Intravenous Solution—Single-Use Vials

TEQUIN Tablets are packaged in bottles, unit dose blister strips, and multidose blister packs of 5 tablets (NDC 0015-1177-21). Tablets are almond shaped and biconvex and contain gatifloxacin sesquihydrate equivalent to either 200 mg or 400 mg of gatifloxacin.

Intravenous Premix in Flexible Containers

Storage

Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Intravenous Solution—Premix Bags

TEQUIN Tablets are packaged in bottles, unit dose blister strips, and multidose blister packs of 5 tablets (NDC 0015-1177-21). Tablets are almond shaped and biconvex and contain gatifloxacin sesquihydrate equivalent to either 200 mg or 400 mg of gatifloxacin.

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Storage

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achieved clinical and bacteriological success post-therapy. The clinical cure rates and bacteriological success were 100% in patients with MDRSP isolates obtained primarily from post-marketing studies of patients with CAP.

**REFERENCES**


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### Table: Clinical and Bacteriological Success Rates for Gatifloxacin-Treated MDRSP Patients (Population: Valid for Efficacy)

<table>
<thead>
<tr>
<th>Screening Susceptibility</th>
<th>Clinical Success</th>
<th>Bacteriological Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin-resistant</td>
<td>10/10 (100%)</td>
<td>10/10 (100%)</td>
</tr>
<tr>
<td>Macrolide-resistant**</td>
<td>24/24 (100%)</td>
<td>24/24 (100%)</td>
</tr>
<tr>
<td>Tetracycline-resistant*</td>
<td>12/12 (100%)</td>
<td>12/12 (100%)</td>
</tr>
</tbody>
</table>

*MDRSP* is Multidrug-Resistant Streptococcus pneumoniae

**: Clarithromycin and erythromycin were the macrolide antimicrobials tested.

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### Table: Clinical Success and Bacteriological Eradication Rates for Gatifloxacin-Treated MDRSP Patients (Population: Valid for Efficacy)

<table>
<thead>
<tr>
<th>Strptococcus pneumoniae with MDRSP</th>
<th>Clinical Success Rate</th>
<th>Bacteriological Eradication Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistant to at least 2 antimicrobials</td>
<td>12/12 (100%)</td>
<td>12/12 (100%)</td>
</tr>
<tr>
<td>Resistant to at least 3 antimicrobials</td>
<td>12/12 (100%)</td>
<td>12/12 (100%)</td>
</tr>
<tr>
<td>Resistant to at least 4 antimicrobials</td>
<td>12/12 (100%)</td>
<td>12/12 (100%)</td>
</tr>
<tr>
<td>Resistant to at least 5 antimicrobials</td>
<td>12/12 (100%)</td>
<td>12/12 (100%)</td>
</tr>
<tr>
<td>Bacteria with MDRSP</td>
<td>3/3 (100%)</td>
<td>3/3 (100%)</td>
</tr>
</tbody>
</table>

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### REFERENCES
