

<b>GATIFLOXACIN (Gfx)</b>	
<b>DRUG CLASS: FLUOROQUINOLONE</b>	
<b>Activity against TB, mechanism of action, and metabolism</b>	<b>Bactericidal:</b> acts by inhibiting the A subunit of DNA gyrase (topoisomerase), which is essential in the reproduction of bacterial DNA. It undergoes limited metabolism and is excreted largely unchanged in the urine with less than 1% as metabolites. A small amount (5%) is also excreted unchanged in the faeces.
<b>Preparation and dose</b>	Tablets, 200 or 400 mg. Vials (20 and 40 ml) or flexible containers (200 and 400 ml) with aqueous or 5% dextrose IV solutions equivalent to 200 and 400 mg. Usual dose: 400 mg/day.
<b>Storage</b>	Room temperature (15–25 °C), airtight containers protected from light.
<b>Oral absorption</b>	Gatifloxacin is readily absorbed from the gastrointestinal tract with an absolute bioavailability of 96%. Should not be administered within 4 h of other medications containing divalent cations (iron, magnesium, zinc, vitamins, didanosine, sucralfate). No interaction with milk or calcium.
<b>Distribution, CSF penetration</b>	Widely distributed in body fluids, including the CSF; tissue penetration is good and approximately 20% appears to be bound to plasma proteins. It crosses the placenta and is distributed into breast milk. It also appears in the bile. Kidney and lung tissue levels exceeded those in serum.
<b>Special circumstances</b>	<b>Pregnancy/breastfeeding:</b> safety class C. Fluoroquinolones are not recommended during breastfeeding due to the potential for arthropathy. Animal data demonstrated arthropathy in immature animals, with erosions in joint cartilage. <b>Renal disease:</b> doses of gatifloxacin should be reduced in patients with renal impairment; When the creatinine clearance is less than 30 ml/min, the recommended dosing is 400 mg 3 times per week.
<b>Adverse effects</b>	Generally well tolerated. <b>Occasional:</b> gastrointestinal intolerance; CNS-headache; malaise; insomnia; restlessness; dizziness; allergic reactions; diarrhoea; photosensitivity; increased LFTs; tendon rupture (increased incidence seen in older men with concurrent use of corticosteroids).
<b>Drug interactions</b>	As gatifloxacin may have the potential to prolong the QT interval, it should not be given to patients receiving class Ia antiarrhythmic drugs (such as quinidine and procainamide) or Class III antiarrhythmics (such as amiodarone and sotalol). In addition, caution should be exercised when gatifloxacin is used with other drugs known to have this effect (such as the antihistamines astemizole and terfenadine, cisapride, erythromycin, pentamidine, phenothiazines, or tricyclic antidepressants). <b>Sucralfate:</b> decreased absorption of fluoroquinolones caused by the chelation by aluminium ions contained in the sucralfate. <b>Antacids</b> (magnesium, aluminium, calcium, Al-Mg buffer found in didanosine): antacid binding to fluoroquinolone antibiotics resulting in decreased absorption and loss of therapeutic efficacy. <b>Probenecid:</b> probenecid interferes with renal tubular secretion of ciprofloxacin; this may result in 50% increase in serum level of ciprofloxacin. <b>Vitamins and minerals</b> containing divalent and trivalent cations such as zinc and iron: formation of fluoroquinolone-ion complex results in decreased absorption of fluoroquinolones.

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<b>Drug interactions</b>	<p><b>Mexiletine:</b> fluoroquinolones may inhibit cytochrome P450 1A2, resulting in increased mexiletine concentration.</p> <p><b>Warfarin:</b> case reports of gatifloxacin enhancing anticoagulation effect of warfarin.</p>
<b>Contraindications</b>	Pregnancy, intolerance of fluoroquinolones.
<b>Monitoring</b>	No laboratory monitoring requirements.
<b>Alerting symptoms</b>	<ul style="list-style-type: none"> <li>— Pain, swelling or tearing of a tendon or muscle or joint pain</li> <li>— Rashes, hives, bruising or blistering, trouble breathing</li> <li>— Diarrhoea</li> <li>— Yellow skin or eyes</li> <li>— Anxiety, confusion or dizziness</li> </ul>

<b>KANAMYCIN (Km)</b>	
<b>DRUG CLASS: AMINOGLYCOSIDE</b>	
<b>Activity against TB, mechanism of action, and metabolism</b>	<b>Bactericidal:</b> aminoglycosides inhibit protein synthesis by irreversibly binding to 30S ribosomal subunit; aminoglycosides are not metabolized in the liver, they are excreted unchanged in the urine.
<b>Distribution</b>	0.2–0.4 l/kg; distributed in extracellular fluid, abscesses, ascitic fluid, pericardial fluid, pleural fluid, synovial fluid, lymphatic fluid and peritoneal fluid. Not well distributed into bile, aqueous humour, bronchial secretions, sputum and CSF.
<b>Preparation and dose</b>	Kanamycin sulfate, sterile powder for intramuscular injection in sealed vials. The powder needs to be dissolved in water for injections before use. The optimal dose is 15 mg/kg body weight, usually 750 mg to 1 g given daily or 5–6 days per week, by deep intramuscular injection. Rotation of injection sites avoids local discomfort. When necessary, it is possible to give the drug at the same total dose 2 or 3 times weekly during the continuation phase, under close monitoring for adverse effects.
<b>Storage</b>	Powder stable at room temperature (15–25 °C), diluted solution should be used the same day.
<b>Oral absorption</b>	There is no significant oral absorption.
<b>CSF penetration</b>	Penetrates inflamed meninges only.
<b>Special circumstances</b>	<p><b>Pregnancy/breastfeeding:</b> safety class D. Eighth cranial nerve damage has been reported following in utero exposure to kanamycin. Excreted in breast milk. The American Academy of Paediatrics considers kanamycin to be compatible with breastfeeding.</p> <p><b>Renal disease:</b> use with caution. Levels should be monitored for patients with impaired renal function. Interval adjustment (12–15 mg/kg 2 or 3 times per week) is recommended for creatinine clearance &lt;30 ml/minute or haemodialysis.</p> <p><b>Hepatic disease:</b> drug levels not affected by hepatic disease (except a larger volume of distribution for alcoholic cirrhotic patients with ascites). Presumed to be safe in severe liver disease; however, use with caution – some patients with severe liver disease may progress rapidly to hepatorenal syndrome.</p>
<b>Adverse effects</b>	<p><b>Frequent:</b> pain at injection site, renal failure (usually reversible).</p> <p><b>Occasional:</b> vestibular and auditory damage – usually irreversible; genetic predisposition possible (check family for aminoglycoside ototoxicity), nephrotoxicity (dose-related to cumulative and peak concentrations, increased risk with renal insufficiency, often irreversible), peripheral neuropathy, rash.</p> <p>Ototoxicity potentiated by certain diuretics (especially loop diuretics), advanced age, and prolonged use. The effect of non-depolarizing muscle relaxants may be increased.</p> <p>Penicillins: in vitro antagonism.</p>
<b>Drug interactions</b>	<p><b>Loop diuretics</b> (bumetanide, furosemide, etacrynic acid, torasemide). Co-administration of aminoglycosides with loop diuretics may have an additive or synergistic auditory ototoxicity. Ototoxicity appears to be dose-dependent and may be increased with renal dysfunction. Irreversible ototoxicity has been reported. Avoid concomitant administration; if used together, careful dose adjustments in patients with renal failure and close monitoring for ototoxicity are required.</p>

**KANAMYCIN (Km)**

**DRUG CLASS: AMINOGLYCOSIDE**

<b>Drug interactions</b>	<p><b>Non-depolarizing muscle relaxants</b> (atracurium, pancuronium, tubocurarine, gallamine triethiodide): possible enhanced action of non-depolarizing muscle relaxant resulting in possible respiratory depression. Avoid co-administration; if concurrent administration is needed, titrate the non-depolarizing muscle relaxant slowly and monitor neuromuscular function closely.</p> <p><b>Nephrotoxic agents</b> (amphotericin B, foscarnet, cidofovir): additive nephrotoxicity. Avoid co-administration; if used together, monitor renal function closely and discontinue if warranted.</p> <p><b>Penicillins:</b> in vitro inactivation (possible). Do not mix together before administration.</p>
<b>Contraindications</b>	<p>Pregnancy (congenital deafness seen with streptomycin and kanamycin use in pregnancy). Hypersensitivity to aminoglycosides. Caution with renal, hepatic, vestibular or auditory impairment.</p>
<b>Monitoring</b>	<p>Monthly creatinine and serum potassium in low-risk patients (young with no co-morbidities), more frequently in high-risk patients (elderly, diabetic, or HIV-positive patients, or patients with renal insufficiency). If potassium is low, check magnesium and calcium. Baseline audiometry and monthly monitoring in high-risk patients. For problems with balance, consider increasing dosing interval.</p>
<b>Alerting symptoms</b>	<ul style="list-style-type: none"> <li>— Problems with hearing; dizziness</li> <li>— Rash</li> <li>— Trouble breathing</li> <li>— Decreased urination</li> <li>— Swelling, pain or redness at injection site</li> <li>— Muscle twitching or weakness</li> </ul>

<b>LEVOFLOXACIN (Lfx)</b>	
<b>DRUG CLASS: FLUOROQUINOLONE</b>	
<b>Activity against TB, mechanism of action, and metabolism</b>	<p><b>Bactericidal:</b> acts by inhibiting the A subunit of DNA gyrase (topoisomerase), which is essential in the reproduction of bacterial DNA.</p> <p>Levofloxacin is generally considered to be about twice as active as its isomer, ofloxacin.</p> <p>Minimal hepatic metabolism; 87% of dose excreted unchanged in the urine within 48 h via glomerular filtration and tubular secretion.</p>
<b>Preparation and dose</b>	<p>Tablets (250, 500, 750 mg).</p> <p>Aqueous solution or solution in 5% dextrose for IV administration – vials (20, 30 ml) 500 or 750 mg and flexible containers (50, 100, 150 ml) 250; 500 or 750 mg.</p> <p>Usual dose: 750 mg/day.</p>
<b>Storage</b>	<p>Tablets: room temperature (15–25 °C), airtight containers protected from light.</p>
<b>Oral absorption</b>	<p>Levofloxacin is rapidly and essentially completely absorbed after oral administration. Orally, should not be administered within 4 h of other medications containing divalent cations (iron, magnesium, zinc, vitamins, didanosine, sucralfate). No interaction with milk or calcium.</p>
<b>Distribution, CSF penetration</b>	<p>Distributes well in blister fluid and lung tissues, also widely distributed (kidneys, gall bladder, gynaecological tissues, liver, lung, prostatic tissue, phagocytic cells, urine, sputum and bile). 30–50% of serum concentration is attained in CSF with inflamed meninges.</p>
<b>Special circumstances</b>	<p><b>Pregnancy/breastfeeding:</b> safety class C. There are no adequate and well-controlled studies in pregnant women. Levofloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Animal data demonstrated arthropathy in immature animals, with erosions in joint cartilage. Because of the potential for serious adverse effects from levofloxacin 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.</p> <p><b>Renal disease:</b> doses of levofloxacin should be reduced in patients with severe renal impairment. When the creatinine clearance is less than 30 ml/minute, the recommended dosing is 750–1000 mg 3 times per week.</p> <p><b>Hepatic disease:</b> given the limited extent of levofloxacin metabolism, the pharmacokinetics of levofloxacin are not expected to be affected by hepatic impairment.</p>
<b>Adverse effects</b>	<p>Generally well tolerated.</p> <p><b>Occasional:</b> gastrointestinal intolerance; CNS-headache; malaise; insomnia; restlessness; dizziness; allergic reactions; diarrhoea; photosensitivity.</p> <p><b>Rare:</b> QT prolongation; tendon rupture; peripheral neuropathy.</p>
<b>Drug interactions</b>	<p>Should not be given to patients receiving class Ia antiarrhythmic drugs (such as quinidine and procainamide) or Class III antiarrhythmics (such as amiodarone and sotalol).</p> <p><b>Sucralfate:</b> decreased absorption of fluoroquinolones caused by the chelation by aluminium ions contained in the sucralfate.</p> <p><b>Antacids</b> (magnesium, aluminium, calcium, Al-Mg buffer found in didanosine): antacid binding to fluoroquinolone antibiotics resulting in decreased absorption and loss of therapeutic efficacy.</p>

**LEVOFLOXACIN (Lfx)****DRUG CLASS: FLUOROQUINOLONE**

<b>Drug interactions</b>	<p><b>Probenecid:</b> probenecid interferes with renal tubular secretion of fluoroquinolones, which may result in 50% increase in serum level of levofloxacin.</p> <p><b>Vitamins and minerals</b> containing divalent and trivalent cations such as zinc and iron. Formation of fluoroquinolone-ion complex results in decreased absorption of fluoroquinolones.</p> <p><b>Mexiletine:</b> fluoroquinolones may inhibit cytochrome P450 1A2 resulting in increased mexiletine concentration.</p>
<b>Contraindications</b>	Pregnancy; hypersensitivity to fluoroquinolones; prolonged QT.
<b>Monitoring</b>	No specific laboratory monitoring requirements.
<b>Alerting symptoms</b>	<ul style="list-style-type: none"> <li>— Pain, swelling or tearing of a tendon or muscle or joint pain</li> <li>— Rashes, hives, bruising or blistering, trouble breathing</li> <li>— Diarrhoea</li> <li>— Yellow skin or eyes</li> <li>— Anxiety, confusion or dizziness</li> </ul>

<b>MOXIFLOXACIN (Mfx)</b>	
<b>DRUG CLASS: FLUOROQUINOLONE</b>	
<b>Activity against TB, mechanism of action, and metabolism</b>	<p><b>Bactericidal:</b> acts by inhibiting the A subunit of DNA gyrase (topoisomerase), which is essential in the reproduction of bacterial DNA.</p> <p>The cytochrome P450 system is not involved in moxifloxacin metabolism, and is not affected by moxifloxacin. Approximately 45% of an oral or intravenous dose of moxifloxacin is excreted as unchanged drug (~20% in urine and ~25% in faeces).</p>
<b>Preparation and dose</b>	Tablets 400 mg and intravenous solution 250 ml–400 mg in 0.8% saline. Usual dose: 400 mg/day.
<b>Storage</b>	Tablets: room temperature (15–25 °C), airtight containers protected from light.
<b>Oral absorption</b>	Moxifloxacin, given as an oral tablet, is well absorbed from the gastro-intestinal tract. The absolute bioavailability of moxifloxacin is approximately 90%. Co-administration with a high fat meal (e.g. 500 calories from fat) does not affect the absorption of moxifloxacin.
<b>Distribution, CSF penetration</b>	Moxifloxacin has been detected in the saliva, nasal and bronchial secretions, mucosa of the sinuses, skin blister fluid, and subcutaneous tissue, and skeletal muscle following oral or intravenous administration of 400 mg.
<b>Special circumstances</b>	<p><b>Pregnancy/breastfeeding:</b> safety class C. Since there are no adequate or well-controlled studies in pregnant women, moxifloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Because of the potential for serious adverse effects in infants nursing from mothers taking moxifloxacin, 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.</p> <p><b>Renal disease:</b> no dosage adjustment is required in renally impaired patients, including those on either haemodialysis or continuous ambulatory peritoneal dialysis.</p> <p><b>Hepatic disease:</b> no dosage adjustment is required in patients with mild or moderate hepatic insufficiency.</p>
<b>Adverse effects</b>	<p>Generally well tolerated.</p> <p><b>Occasional:</b> gastrointestinal intolerance; CNS-headache; malaise; insomnia; restlessness; dizziness; allergic reactions; diarrhoea; photosensitivity. Moxifloxacin has been found in isolated cases to prolong the QT interval.</p>
<b>Drug interactions</b>	<p>Should not be given to patients receiving class Ia antiarrhythmic drugs (such as quinidine and procainamide) or class III antiarrhythmics (such as amiodarone and sotalol).</p> <p><b>Sucralfate:</b> decreased absorption of fluoroquinolones caused by the chelation by aluminium ions contained in the sucralfate.</p> <p><b>Antacids</b> (magnesium, aluminium, calcium, Al-Mg buffer found in didanosine): antacid binding to fluoroquinolone antibiotics resulting in decreased absorption and loss of therapeutic efficacy.</p> <p><b>Vitamins and minerals</b> containing divalent and trivalent cations such as zinc and iron: formation of fluoroquinolone-ion complex results in decreased absorption of fluoroquinolones.</p>
<b>Contraindications</b>	Pregnancy; hypersensitivity to fluoroquinolones; prolonged QT.
<b>Monitoring</b>	No specific laboratory monitoring requirements.

**MOXIFLOXACIN (Mfx)**

**DRUG CLASS: FLUOROQUINOLONE**

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**Alerting symptoms**

- Pain, swelling or tearing of a tendon or muscle or joint pain
  - Rashes, hives, bruising or blistering, trouble breathing
  - Diarrhoea
  - Yellow skin or eyes
  - Anxiety, confusion or dizziness
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<b>OFLOXACIN (Ofx)</b>	
<b>DRUG CLASS: FLUOROQUINOLONES</b>	
<b>Activity against TB, mechanism of action, and metabolism</b>	<p><b>Bactericidal:</b> acts by inhibiting the A subunit of DNA gyrase (topoisomerase), which is essential in the reproduction of bacterial DNA.</p> <p>There is no cross-resistance with other antituberculosis agents, but complete cross-resistance between ofloxacin and ciprofloxacin. There is limited metabolism to desmethyl and N-oxide metabolites; desmethylofloxacin has moderate antibacterial activity. Ofloxacin is eliminated mainly by the kidneys. Excretion is by tubular secretion and glomerular filtration and 65–80% of a dose is excreted unchanged in the urine over 24–48 hours, resulting in high urinary concentrations.</p>
<b>Preparation and dose</b>	Tablets (200, 300 or 400 mg). Vials (10 ml) or flexible containers (50 and 100 ml) with aqueous or 5% dextrose IV solutions equivalent to 200 and 400 mg. Usual dose: 400 mg twice daily.
<b>Storage</b>	Room temperature (15–25 °C), airtight containers protected from light.
<b>Oral absorption</b>	90–98% oral absorption.
<b>Distribution, CSF penetration</b>	About 25% is bound to plasma proteins. Ofloxacin is widely distributed in body fluids, including the CSF, and tissue penetration is good. It crosses the placenta and is distributed into breast milk. It also appears in the bile.
<b>Special circumstances</b>	<p><b>Pregnancy/breastfeeding:</b> usually compatible with breastfeeding.</p> <p><b>Renal disease:</b> doses of ofloxacin should be reduced in patients with severe renal impairment. When the creatinine clearance is less than 30 ml/minute, the recommended dosing is 600–800 mg 3 times per week.</p>
<b>Adverse effects</b>	<p>Generally well tolerated.</p> <p><b>Occasional:</b> gastrointestinal intolerance; CNS-headache, malaise, insomnia, restlessness, and dizziness.</p> <p><b>Rare:</b> allergic reactions; diarrhoea; photosensitivity; increased LFTs; tendon rupture; peripheral neuropathy.</p>
<b>Drug interactions</b>	Fluoroquinolones are known to inhibit hepatic drug metabolism and may interfere with the clearance of drugs such as theophylline and caffeine that are metabolized by the liver. Cations such as aluminium, magnesium or iron reduce the absorption of ofloxacin and related drugs when given concomitantly. Changes in the pharmacokinetics of fluoroquinolones have been reported when given with histamine H2 antagonists, possibly due to changes in gastric pH, but do not seem to be of much clinical significance. The urinary excretion of ofloxacin and some other fluoroquinolones is reduced by probenecid; plasma concentrations are not necessarily increased.
<b>Contraindications</b>	Pregnancy, intolerance of fluoroquinolones.
<b>Monitoring</b>	No specific laboratory monitoring requirements.
<b>Alerting symptoms</b>	<ul style="list-style-type: none"> <li>— Pain, swelling or tearing of a tendon or muscle or joint pain</li> <li>— Rashes, hives, bruising or blistering, trouble breathing</li> <li>— Diarrhoea</li> <li>— Yellow skin or eyes</li> <li>— Anxiety, confusion or dizziness</li> </ul>

**P-AMINOSALICYLIC ACID (PAS)**

DRUG CLASS: SALICYLIC ACID; ANTI-FOLATE

<b>Activity against TB, mechanism of action, and metabolism</b>	<b>Bacteriostatic:</b> disrupts folic acid metabolism. Acetylated in the liver to <i>N</i> -acetyl- <i>p</i> -aminosalicylic acid and <i>p</i> -aminosalicylic acid, which are excreted via glomerular filtration and tubular secretion.
<b>Preparation and dose</b>	Tablets, sugar-coated, containing sodium salt: sodium <i>p</i> -aminosalicylate, 0.5 g of PAS. Granules of PAS with an acid-resistant outer coating rapidly dissolved in neutral media, 4 g per packet. 150 mg/kg or 10–12 g daily in 2 divided doses. Children: 200–300 mg/kg daily in 2–4 divided doses.
<b>Storage</b>	Packets should be kept in the refrigerator or freezer. Other formulations may not require refrigeration (consult manufacturer's recommendations).
<b>Oral absorption</b>	Incomplete absorption (usually 60–65%): sometimes requires increased doses to achieve therapeutic levels.
<b>Distribution, CSF penetration</b>	Distributed in peritoneal fluid, pleural fluid, synovial fluid. Not well distributed in CSF (10–15%) and bile.
<b>Special circumstances</b>	<b>Pregnancy/breastfeeding:</b> safety class C. Congenital defects in babies have been reported with exposure to PAS in the first trimester. PAS is secreted into human breast milk (1/70th of maternal plasma concentration). <b>Renal disease:</b> no dose adjustment is recommended. However, PAS can exacerbate acidosis associated with renal insufficiency and if possible should be avoided in patients with severe renal impairment due to crystalluria. Sodium PAS should also be avoided in patients with severe renal impairment.
<b>Adverse effects</b>	<b>Frequent:</b> gastrointestinal intolerance (anorexia and diarrhoea); hypo-thyroidism (increased risk with concomitant use of ethionamide). <b>Occasional:</b> hepatitis (0.3–0.5%); allergic reactions; thyroid enlargement; malabsorption syndrome; increased prothrombin time; fever. Careful use in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.
<b>Drug interactions</b>	<b>Digoxin:</b> possible decrease in digoxin absorption; monitor digoxin level – may need to be increased. <b>Ethionamide:</b> possible increase in liver toxicity, monitor liver enzymes; hypothyroidism in case of combined administration. <b>Isoniazid:</b> decreased acetylation of isoniazid resulting in increased isoniazid level. Dose may need to be decreased.
<b>Contraindications</b>	Allergy to aspirin; severe renal disease; hypersensitivity to the drug.
<b>Monitoring</b>	Monitor TSH, electrolytes, blood counts, and liver function tests.
<b>Alerting symptoms</b>	— Skin rash, severe itching, or hives — Severe abdominal pain, nausea or vomiting — Unusual tiredness or loss of appetite — Black stools as a result of intestinal bleeding