

Fluoroquinolones

Bactericidal inhibitors of bacterial DNA topoisomerases that cause permanent chromosomal breaks, carrying some of the most serious safety warnings of any antibiotic class.

Online guide: <https://www.medguideglobal.com/pharmacology/antibiotics/fluoroquinolones>

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Quick revision

One Liner: Fluoroquinolones trap bacterial topoisomerases on DNA, turning them into a source of permanent double-stranded chromosomal breaks - highly effective, and carrying warnings serious enough to make them a considered choice rather than a default.

1. Mechanism: inhibit DNA ligation and stabilise enzyme-DNA complexes, producing permanent double-stranded breaks in the bacterial chromosome. [1]
2. Bactericidal - the organism is overwhelmed because it cannot repair the damage. [1]
3. Six agents have FDA approval for systemic use: moxifloxacin, ciprofloxacin, gemifloxacin, levofloxacin, delafloxacin and ofloxacin. [1]
4. Ciprofloxacin is not a drug of first choice for pneumococcal pneumonia, even though it has some activity against *Streptococcus pneumoniae*; levofloxacin is the one with enhanced gram-positive activity including *S. pneumoniae*. [1][4][2]
5. Moxifloxacin has poor *Pseudomonas* activity but covers anaerobes. [1]
6. Delafloxacin is the only agent in the class with an approved indication covering MRSA, and the only one whose activity against it is reliable. [1]
7. Serious warnings include tendon rupture, peripheral neuropathy, QTc prolongation, aortic aneurysm and dissection, and CNS effects. [1]
8. Relatively contraindicated in pregnancy and in children, because of cartilage damage and arthropathy risk. [1]

Overview

1. Fluoroquinolones are bactericidal agents that target bacterial DNA topoisomerases. Rather than simply blocking an enzyme, they inhibit DNA ligation and stabilise the enzyme-DNA complex, which produces permanent double-stranded breaks in the bacterial chromosome and overwhelms the organism's capacity to repair them. [1]
2. Six quinolones currently hold FDA approval for systemic use - moxifloxacin, ciprofloxacin, gemifloxacin, levofloxacin, delafloxacin and ofloxacin - representing successive generations with expanding coverage. The agents are not interchangeable: their differences in gram-positive, *Pseudomonas*, anaerobic and MRSA activity are the reason a specific fluoroquinolone is chosen rather than any fluoroquinolone. [1]
3. The class is also defined by its safety profile. Tendon rupture, peripheral neuropathy, QTc prolongation, aortic aneurysm and dissection, central nervous system effects and a recognised disability syndrome together make fluoroquinolones a class where the decision to use one is weighed against alternatives rather than taken by default. [1]

Classification and drug examples

Intro: The useful split is not by generation number but by what each agent actually covers: gram-negative reach, respiratory gram-positive cover, anaerobic cover, and MRSA.

1. Name: Gram-negative-focused agents

1. Note: Strongest against gram-negative bacilli; *Streptococcus pneumoniae* is the weak point, and ciprofloxacin is not a first choice for pneumococcal pneumonia.

1. Name: Ciprofloxacin

1. Route: Oral/IV

1. Note: The most potent of the class against gram-negative bacilli including *Escherichia coli*, *Salmonella*, *Shigella* and *Neisseria*; not a drug of first choice where *S. pneumoniae* is the likely pathogen. [3][1][2]

2. Name: Ofloxacin

2. Route: Oral

2. Note: One of the six agents FDA-approved for systemic use. [1] [3][1]

2. Name: Respiratory fluoroquinolones

2. Note: Enhanced gram-positive activity, which is what makes them usable where pneumococcal cover is needed.

1. Name: Levofloxacin

1. Route: Oral/IV

1. Note: Most enhanced activity against penicillin-sensitive and penicillin-resistant gram-positive organisms, notably *S. pneumoniae*; reduced *Pseudomonas* action compared with ciprofloxacin. [4]

2. Name: Moxifloxacin

2. Route: Oral/IV

2. Note: Poor *Pseudomonas* activity but covers anaerobes. [1]

3. Name: Gemifloxacin

3. Route: Oral

3. Note: One of the six agents FDA-approved for systemic use. [1] [4][1]

3. Name: Anti-MRSA fluoroquinolone

3. Note: A single agent, and the only member of the class with an approved MRSA indication.

Name: Delafloxacin

Route: Oral/IV

Note: The only fluoroquinolone with an approved indication covering MRSA. [1] [1]

Mechanism of action

Summary: Fluoroquinolones target bacterial DNA topoisomerases, inhibiting DNA ligation and stabilising the enzyme-DNA complex so that permanent double-stranded breaks accumulate in the bacterial chromosome.

Target: Bacterial DNA topoisomerases (DNA gyrase and topoisomerase IV)

Cidal Static: bactericidal

Kill Kinetics: concentration-dependent

1. Step: 1

1. Title: The drug binds the topoisomerase-DNA complex

1. Detail: Quinolones target bacterial DNA topoisomerases while those enzymes are engaged with DNA. [1]

2. Step: 2

2. Title: DNA ligation is inhibited

2. Detail: The enzyme can cut the DNA but can no longer rejoin it. [1]

3. Step: 3

3. Title: The complex is stabilised

3. Detail: Trapping the enzyme on the DNA converts a normal repair intermediate into permanent damage. [1]

4. Step: 4

4. Title: Double-stranded breaks accumulate

4. Detail: Permanent double-stranded breaks build up in the bacterial chromosome. [1]

5. Step: 5

5. Title: Repair capacity is overwhelmed and the cell dies

5. Detail: By preventing DNA repair, the drugs overwhelm the organism's repair capacity and cause bacterial cell death.

[1]

Spectrum of activity

Intro: Learn this class agent by agent. The differences between members - pneumococcal cover, Pseudomonas, anaerobes, MRSA - are exactly what the exam and the prescribing decision turn on.

1. Subclass Id: gram-negative-focused

1. Gram-negative bacilli

2. Enterobacteriaceae: E. coli, Salmonella, Shigella

3. Neisseria

Streptococcus pneumoniae [3][1]

2. Subclass Id: respiratory

Penicillin-sensitive and penicillin-resistant S. pneumoniae (levofloxacin)

Gram-negative cover, reduced against Pseudomonas relative to ciprofloxacin

Anaerobes (moxifloxacin)

Pseudomonas aeruginosa (moxifloxacin) [4][1]

3. Subclass Id: anti-mrsa

MRSA

Gram-negative cover [1]

Major clinical uses

1. Drug: Ciprofloxacin

1. Organism: Gram-negative urinary pathogens

1. Indication: Urinary tract infection

1. Line: targeted

1. Note: Also FDA-approved for prostatitis, typhoid fever, gastrointestinal infection, anthrax, plague and salmonellosis. [3]

2. Drug: Levofloxacin

2. Organism: Streptococcus pneumoniae

2. Indication: Pneumonia

2. Line: targeted

2. Note: Its enhanced gram-positive activity is what makes it usable here where ciprofloxacin is not. [4][1]

3. Drug: Ciprofloxacin

3. Organism: Neisseria gonorrhoeae and other susceptible organisms

3. Indication: Sexually transmitted infection, including gonorrhoea and chancroid

3. Line: targeted

3. Note: An FDA-approved indication; local resistance patterns govern whether it remains appropriate. [3]

4. Drug: Fluoroquinolones as a class

4. Organism: Susceptible organisms

4. Indication: Bone and joint infection, intra-abdominal infection

4. Line: targeted

4. Note: Approved uses across the class. [1]

5. Drug: Moxifloxacin

5. Organism: Anaerobes and susceptible gram-positives

5. Indication: Infection where anaerobic cover is wanted without Pseudomonas

5. Line: targeted

5. Note: Its anaerobic cover distinguishes it within the class. [1]

6. Drug: Fluoroquinolones as a class

6. Organism: Mycobacterium tuberculosis

- 6. Indication: Drug-resistant tuberculosis
- 6. Line: off-label
- 6. Note: An off-label application under specialist direction. [1]

Pharmacokinetics

- 1. Drug: Ciprofloxacin
- 1. Route: Oral/IV
- 1. Absorption: Orally available
- 1. Csf Penetration: See prescribing reference
- 1. Metabolism: See prescribing reference
- 1. Elimination: See prescribing reference
- 1. Half Life: See prescribing reference
- 1. Dose Adjust: See prescribing reference [3]
- 2. Drug: Levofloxacin
- 2. Route: Oral/IV
- 2. Absorption: Orally available
- 2. Csf Penetration: See prescribing reference
- 2. Metabolism: See prescribing reference
- 2. Elimination: See prescribing reference
- 2. Half Life: See prescribing reference
- 2. Dose Adjust: See prescribing reference [4]
- 3. Drug: Moxifloxacin
- 3. Route: Oral/IV
- 3. Absorption: Orally available
- 3. Csf Penetration: See prescribing reference
- 3. Metabolism: See prescribing reference
- 3. Elimination: See prescribing reference
- 3. Half Life: See prescribing reference
- 3. Dose Adjust: See prescribing reference [1]
- 1. Good oral availability is part of why this class was historically over-used: an oral agent with broad cover is convenient, which is precisely the pressure the serious safety warnings are meant to counterbalance. [1]
- 2. This page gives no dose regimens by design. Doses depend on indication, organism, renal function, age and weight, and belong in a prescribing reference used by the treating clinician.

Adverse effects

Effect: Central nervous system effects

Detail: Confusion, anxiety and depression are documented CNS effects of the class. [1]

- 1. Effect: Tendon rupture
 - 1. Detail: Particularly the Achilles tendon, and often bilateral.
 - 1. Action: The drug is stopped and the tendon assessed when new tendon pain or swelling develops. [1]
- 2. Effect: Peripheral neuropathy
 - 2. Detail: Peripheral neuropathy and nerve damage are recognised serious risks.
 - 2. Action: New numbness, tingling or weakness prompts clinical assessment. [1]
- 3. Effect: QTc prolongation
 - 3. Detail: Prolongation of the QTc interval with a risk of Torsades de pointes.
 - 3. Action: Assess QT risk and concurrent QT-prolonging drugs before use. [1]
- 4. Effect: Aortic aneurysm and dissection

4. Detail: A documented serious vascular risk of the class.
4. Action: Treat sudden severe chest, back or abdominal pain as an emergency. [1]
5. Effect: Fluoroquinolone-associated disability syndrome
5. Detail: A recognised syndrome of persisting disabling effects.
5. Action: Symptoms persisting after the course has finished are reviewed clinically. [1]

Contraindications, precautions and interactions

1. Pregnancy, where the class is relatively contraindicated over theoretical concerns about fetal DNA synthesis. [1]
2. Children, where use is restricted because of cartilage damage and arthropathy risk. [1]
3. Existing QT prolongation or concurrent QT-prolonging therapy, given the Torsades de pointes risk. [1]

With: Other QT-prolonging drugs

Effect: Additive QTc prolongation increases the risk of Torsades de pointes. [1]

Resistance mechanisms

1. Mechanism: Target-mediated resistance
 1. Detail: Mutations in the target enzymes themselves reduce quinolone binding.
 1. Countermeasure: Susceptibility-directed therapy. [1]
 2. Mechanism: Plasmid-mediated resistance
 2. Detail: Resistance determinants transferred horizontally between organisms.
 2. Countermeasure: Stewardship to limit selection pressure, plus susceptibility testing. [1]
 3. Mechanism: Chromosome-mediated resistance
 3. Detail: Altered porins or over-expression of efflux pumps reduce how much drug reaches the target.
 3. Countermeasure: Susceptibility-directed therapy. [1]
- Stewardship Note: Because resistance arises by three independent routes including horizontally transferable plasmids, fluoroquinolone resistance spreads readily - one more reason the class is reserved rather than used as a convenient oral default.

Comparison tables

Title: Which fluoroquinolone covers what

Caption: The differences that decide agent choice. Local susceptibility data governs actual therapy.

1. Key: drug
 1. Label: Drug
 1. Is Row Header: true
 2. Key: pneumococcus
 2. Label: S. pneumoniae
 3. Key: pseudomonas
 3. Label: Pseudomonas
 4. Key: anaerobes
 4. Label: Anaerobes
 5. Key: mrsa
 5. Label: MRSA
1. Drug: Ciprofloxacin
 1. Pneumococcus: Not first choice
 1. Pseudomonas: Strongest of the class
 1. Anaerobes: No
 1. Mrsa: No [1][3]

- 2. Drug: Levofloxacin
- 2. Pneumococcus: Yes - most enhanced in the class
- 2. Pseudomonas: Reduced vs ciprofloxacin
- 2. Anaerobes: No
- 2. Mrsa: No [4]
- 3. Drug: Moxifloxacin
- 3. Pneumococcus: Yes
- 3. Pseudomonas: Poor
- 3. Anaerobes: Yes
- 3. Mrsa: No [1]
- 4. Drug: Delafloxacin
- 4. Pneumococcus: Yes
- 4. Pseudomonas: See prescribing reference
- 4. Anaerobes: See prescribing reference
- 4. Mrsa: Yes - the only one [1]

High-yield exam pearls

- 1. Pearl: The class kills by weaponising the enzyme, not just blocking it.
- 1. Why: Fluoroquinolones stabilise the enzyme-DNA complex, so the topoisomerase itself becomes the source of permanent double-stranded chromosomal breaks. [1]
- 2. Pearl: Ciprofloxacin is the gram-negative one; levofloxacin is the respiratory one.
- 2. Why: Ciprofloxacin is the most potent of the class against gram-negative bacilli including Enterobacteriaceae; levofloxacin has the most enhanced gram-positive activity, notably against *S. pneumoniae*, with reduced *Pseudomonas* action compared with ciprofloxacin. [3][4]
- 3. Pearl: Moxifloxacin trades *Pseudomonas* for anaerobes.
- 3. Why: It has poor *Pseudomonas* activity but covers anaerobes - the opposite trade-off from ciprofloxacin. [1]
- 4. Pearl: Delafloxacin is the MRSA fluoroquinolone.
- 4. Why: It is the only member with an approved indication covering methicillin-resistant *Staphylococcus aureus*; most MRSA isolates are resistant to the other fluoroquinolones. [1]
- 5. Pearl: Achilles tendon rupture is the signature adverse effect, and it is often bilateral.
- 5. Why: Tendon rupture is among the class's most recognised serious warnings, with the Achilles tendon particularly affected. [1]
- 6. Pearl: Aortic aneurysm and dissection sits alongside the musculoskeletal warnings.
- 6. Why: It is a documented serious risk of the class and a frequently missed exam point. [1]

Common exam traps

- 1. Trap: "Ciprofloxacin is a good choice for community-acquired pneumonia."
- 1. Correction: Ciprofloxacin's label names *Streptococcus pneumoniae* among the organisms it covers, but states it is not a drug of first choice for pneumococcal pneumonia. Levofloxacin is the agent with enhanced activity against penicillin-sensitive and penicillin-resistant *S. pneumoniae*. [1][4]
- 2. Trap: "All fluoroquinolones cover *Pseudomonas*."
- 2. Correction: Moxifloxacin has poor *Pseudomonas* activity, and levofloxacin has reduced action against *Pseudomonas* compared with ciprofloxacin. [1][4]
- 3. Trap: "Fluoroquinolones are a safe convenient oral option for children."
- 3. Correction: Paediatric use is restricted because of cartilage damage and arthropathy concerns, and the class is relatively contraindicated in children. [1]
- 4. Trap: "The tendon warning is the only serious one."

4. Correction: The class also carries warnings for peripheral neuropathy, QTc prolongation with Torsades de pointes risk, aortic aneurysm and dissection, CNS effects, and fluoroquinolone-associated disability. [1]

Self-test questions

1. Question: What distinguishes the fluoroquinolone mechanism from straightforward enzyme blockade?

1. They occupy the 50S ribosomal subunit and arrest peptide elongation
2. They inhibit DNA ligation and stabilise the enzyme-DNA complex, so the trapped topoisomerase becomes the source of permanent double-stranded chromosomal breaks
3. They deplete the bacterial folate pool and starve the cell of thymidine
4. They insert into the cytoplasmic membrane and collapse the proton gradient

1. Explanation: The enzyme is not merely switched off - it is turned against the cell. Bacterial DNA topoisomerases are caught mid-reaction, able to cut the chromosome but no longer to rejoin it, and what would normally be a transient repair intermediate becomes fixed damage. Double-stranded breaks then accumulate faster than the organism can repair them, which is why killing follows. [1]

2. Question: Why is ciprofloxacin the wrong member of the class when *Streptococcus pneumoniae* is the likely pathogen?

1. Its label states it is not a drug of first choice for pneumococcal pneumonia, whereas levofloxacin is the agent with enhanced activity against both penicillin-sensitive and penicillin-resistant strains
2. It is destroyed by a pneumococcal beta-lactamase
3. It has no oral formulation, which makes respiratory use impractical
4. *S. pneumoniae* is an anaerobe, and no member of the class reaches anaerobes

2. Explanation: Ciprofloxacin's strength lies among the gram-negative bacilli, and the pneumococcus is its weak point rather than an absolute gap - its label names the organism but tells prescribers it is not a first choice for pneumococcal pneumonia. Levofloxacin is the member whose gram-positive activity is most enhanced, extending to penicillin-resistant pneumococci, which is exactly why the two agents are not interchangeable for a chest infection. [1][4]

3. Question: Which statement about anti-pseudomonal activity within this class is correct?

1. Every member provides dependable cover against *Pseudomonas*
2. Moxifloxacin has the strongest *Pseudomonas* activity of the class
3. Moxifloxacin's *Pseudomonas* activity is poor, and levofloxacin's is reduced compared with ciprofloxacin
4. Delafloxacin is the sole member with any *Pseudomonas* activity

3. Explanation: Treating the class as uniformly anti-pseudomonal is a common error. Ciprofloxacin sits at the top for this organism, levofloxacin's action against it is diminished by comparison, and moxifloxacin is weak here - moxifloxacin's distinguishing asset is anaerobic cover instead, the reverse of the ciprofloxacin trade-off. [1][4]

4. Question: Which fluoroquinolone is described as active against methicillin-resistant *Staphylococcus aureus*?

1. Ciprofloxacin
2. Levofloxacin
3. Moxifloxacin
4. Delafloxacin

4. Explanation: Delafloxacin stands alone here: it is the single member of the class credited with MRSA activity, and no other agent among the six approved for systemic use shares it. Moxifloxacin is the one remembered for anaerobic cover, not for resistant staphylococci. [1]

5. Question: Beyond tendon rupture, which group of serious warnings belongs to the fluoroquinolones?

1. Peripheral neuropathy, QTc prolongation with a risk of Torsades de pointes, aortic aneurysm and dissection, central nervous system effects, and a recognised disability syndrome
2. Agranulocytosis, aplastic anaemia and grey baby syndrome
3. Irreversible cochlear hearing loss together with acute renal tubular injury

4. Pulmonary fibrosis, orange discolouration of body secretions and a disulfiram-like reaction
5. Explanation: Treating the tendon warning as the whole story is a frequent slip. Nerve damage, QTc lengthening, the vascular risk of aortic aneurysm and dissection, and the persisting disability syndrome all sit alongside it, and confusion, anxiety and depression are documented central nervous system effects of the class. Taken together these warnings are why a member of this class is a weighed decision rather than a default. [1]
6. Question: Which description of the class's signature musculoskeletal adverse effect is accurate?
 1. A self-limiting myalgia confined to the proximal shoulder girdle
 2. Tendon rupture, with the Achilles tendon particularly affected and involvement frequently bilateral
 3. An erosive arthritis restricted to the small joints of the hand
 4. Osteonecrosis of the jaw after prolonged courses
6. Explanation: Rupture of a tendon is the effect most closely identified with this class, and the Achilles is the classic site. The point students most often miss is that both sides may go, so new tendon pain or swelling calls for the drug to be stopped and assessment sought. [1]
7. Question: On what grounds is this class relatively contraindicated in children and in pregnancy?
 1. Kernicterus from bilirubin displacement in the newborn, and neural tube defects in early pregnancy
 2. Permanent discolouration of developing teeth and impaired bone growth
 3. Cartilage damage and arthropathy in children, alongside a theoretical concern about fetal DNA synthesis in pregnancy
 4. Neonatal haemolytic anaemia and premature closure of the ductus arteriosus
7. Explanation: Paediatric restriction rests on the risk of damage to cartilage and the arthropathies that follow. In pregnancy the reservation is different in kind - a theoretical worry about the drug's action on fetal DNA synthesis - but both place the class in the relatively contraindicated category rather than making it a convenient oral option. [1]
8. Question: By which routes does resistance to this class arise?
 1. Only by enzymatic destruction of the drug, through quinolone-hydrolysing esterases
 2. Mutation of the target enzymes, plasmid-mediated transfer of resistance determinants, and chromosomal change such as altered porins or over-expressed efflux pumps
 3. Post-transcriptional methylation of 23S ribosomal RNA
 4. Acquisition of an alternative penicillin-binding protein with low drug affinity
8. Explanation: Three independent routes are described: the target enzymes themselves mutate so the drug binds less well; determinants move horizontally between organisms on plasmids; and chromosomal changes cut how much drug reaches the target by altering porins or amplifying efflux. Horizontal transfer in particular lets resistance spread readily, which is a further argument for reserving the class rather than using it freely. [1]

Frequently asked questions

1. Question: How do fluoroquinolones actually kill bacteria?
 1. Answer: They trap bacterial topoisomerases on DNA. By inhibiting DNA ligation and stabilising the enzyme-DNA complex they turn a normal repair intermediate into permanent double-stranded chromosomal breaks, and the organism cannot repair fast enough to survive. [1]
 2. Question: What is the practical difference between ciprofloxacin and levofloxacin?
 2. Answer: Ciprofloxacin is the most potent of the class against gram-negative bacilli, but its label states it is not a drug of first choice for pneumococcal pneumonia. Levofloxacin has the most enhanced gram-positive activity, including penicillin-resistant *S. pneumoniae*, with reduced *Pseudomonas* action compared with ciprofloxacin. [3][4]
 3. Question: Why are fluoroquinolones avoided in children?
 3. Answer: Paediatric use is restricted because of concerns about cartilage damage and arthropathies, which makes the class relatively contraindicated in children. [1]
 4. Question: Which fluoroquinolone works against MRSA?
 4. Answer: Delafloxacin, and it is the only member of the class with an approved indication covering MRSA. [1]

5. Question: What are the serious warnings students are expected to know?

5. Answer: Tendon rupture - especially the Achilles, often bilateral - peripheral neuropathy, QTc prolongation with Torsades de pointes risk, aortic aneurysm and dissection, CNS effects such as confusion, anxiety and depression, and fluoroquinolone-associated disability syndrome. [1]

References

[1] Quinolones (StatPearls). StatPearls Publishing / NCBI Bookshelf 2023. <https://www.ncbi.nlm.nih.gov/books/NBK557777/>

[2] CIPRO (ciprofloxacin) - prescribing information. DailyMed, U.S. National Library of Medicine .

<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f406e796-17d9-4465-b8a7-00d966a4ba74>

[3] Ciprofloxacin (StatPearls). StatPearls Publishing / NCBI Bookshelf 2023. <https://www.ncbi.nlm.nih.gov/books/NBK535454/>

[4] Levofloxacin (StatPearls). StatPearls Publishing / NCBI Bookshelf 2023. <https://www.ncbi.nlm.nih.gov/books/NBK545180/>

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