Urinary tract anti-infective agents

Urinary Tract Infections (UTIs)

- Urinary tract infections (UTIs) occur when **microorganisms, primarily bacteria**, invade the urinary system, which includes the **kidneys, ureters, bladder, and urethra**.
- UTIs are more common in **women** than in men.

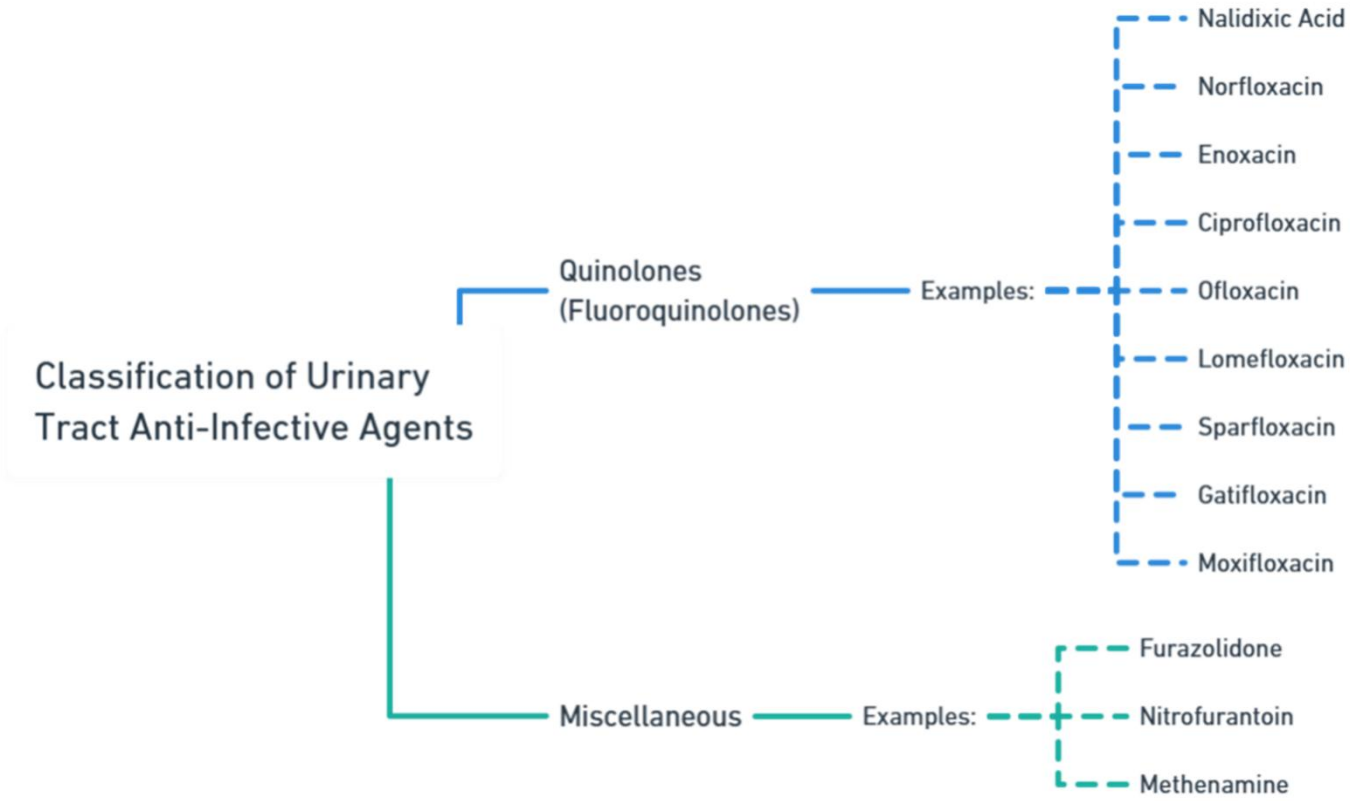
Symptoms of UTIs

Symptoms vary based on the location of the infection:

1. **Lower Urinary Tract Infection (Cystitis, Urethritis)**
   - **Dysuria** (pain or burning sensation during urination)
   - Frequent urination and urgency
   - Cloudy, dark, bloody, or foul-smelling urine
   - Lower abdominal or pelvic discomfort
   - Feeling of incomplete bladder emptying
2. **Upper Urinary Tract Infection (Pyelonephritis)**
   - Flank or back pain
   - High fever, chills
   - Nausea, vomiting
   - Fatigue or weakness
   - **Dysuria, frequency, urgency** (similar to lower UTI symptoms)

Urinary Tract Anti-Infective Agents

- Urinary tract anti-infective agents are used to treat bacterial infections of the urinary tract, such as cystitis, pyelonephritis, and urethritis.
- These agents are classified based on their mechanism of action and chemical structure.



1. Quinolones (Fluoroquinolones)

- These drugs act by inhibiting bacterial DNA gyrase and topoisomerase IV, leading to DNA damage and bacterial cell death.
- **Examples:**
  - Nalidixic Acid
  - Norfloxacin
  - Enoxacin
  - Ciprofloxacin*
  - Ofloxacin
  - Lomefloxacin
  - Sparfloxacin
  - Gatifloxacin
  - Moxifloxacin

SAR Summary of Quinolones

Position	Structural Feature	SAR Insight
C1	N-substitution (e.g., cyclopropyl, ethyl)	Cyclopropyl enhances Gram-positive activity and broadens spectrum (e.g., ciprofloxacin).
C3 & C4	Carboxylic acid and ketone	Essential for binding to bacterial DNA-topoisomerase complex via Mg^{2+}

		bridge. Any modification reduces activity.
C5	H or $-NH_2$ / –OH	Substitutions can enhance Gram-positive activity (e.g., OH improves activity but may increase toxicity).
C6	Fluorine atom (F)	Enhances lipophilicity, cell penetration, and enzyme inhibition. Characteristic of fluoroquinolones.
C7	Piperazine or similar heterocyclic ring	Enhances activity against Gram-negative bacteria. Affects CNS side effects and resistance.
C8	Methoxy or halogen (F, Cl)	Affects phototoxicity and anaerobic activity. Methoxy at C8 (e.g., moxifloxacin) reduces phototoxicity.

2. Miscellaneous Urinary Tract Anti-Infectives

- These agents have varied mechanisms of action, including inhibition of bacterial enzymes, induction of oxidative stress, and acidification of urine, which suppress bacterial growth.
- Examples:
  - Furazolidone
  - Nitrofurantoin*
  - Methenamine

Brand Names Of Important Marketed Products

Used for treating urinary tract infections (UTIs).

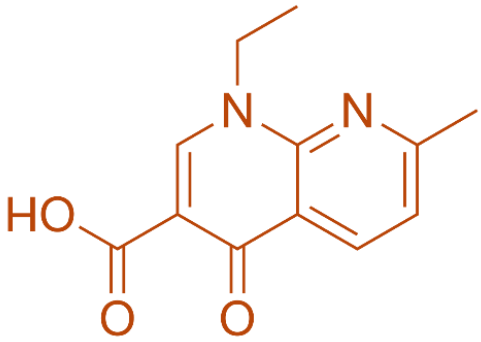
Drug Name	Brand Name(s)	Formulation	Use
Nitrofurantoin	**Macrobid, Furadantin, Niftas**	Capsule	Acute and chronic UTIs
Norfloxacin	**Noroxin, Norilet**	Tablet	Lower UTIs
Fosfomycin	**Monurol, Fomycin**	Sachet (single dose)	Acute uncomplicated UTI
Trimethoprim + Sulfamethoxazole	**Bactrim, Septra**	Tablet, Injection	UTIs and other infections
Ciprofloxacin	**Cipro, Ciplox**	Tablet, IV	Broad spectrum for UTIs

Various Quinolones Drug

1. Nalidixic Acid

Chemical Structure / Formula

- **Formula:** C12H12N2O3
- **Structure:** 1,8-naphthyridine core with a **carboxyl (-COOH) and ketone (-C=O) functional group**.



Mechanism of Action

- Inhibits DNA gyrase (topoisomerase II) and topoisomerase IV, preventing bacterial DNA replication.
- Bactericidal effect due to DNA fragmentation and inhibition of supercoiling.

Uses

- First-generation quinolone used primarily for urinary tract infections (UTIs) caused by E. coli, Proteus, Klebsiella.
- Not used for systemic infections (poor penetration).

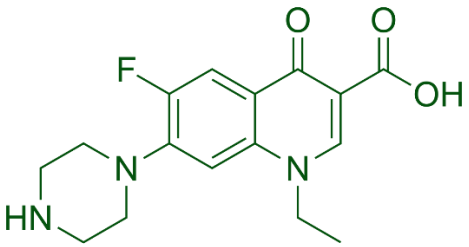
Side Effects

- GI upset (nausea, vomiting, diarrhea).
- CNS effects (dizziness, headache, confusion in elderly patients).
- Photosensitivity.
- Rare: hemolytic anemia in G6PD deficiency.

2. Norfloxacin

Chemical Structure / Formula

- **Formula:** C16H18FN3O3
- **Structure:** A **fluorinated quinolone** (fluoroquinolone), improving potency and spectrum.



Mechanism of Action

- Inhibits DNA gyrase and topoisomerase IV, leading to bacterial DNA fragmentation and death.

Uses

- Used for UTIs, prostatitis, and some GI infections (traveler's diarrhea).
- Limited systemic use due to poor tissue penetration.

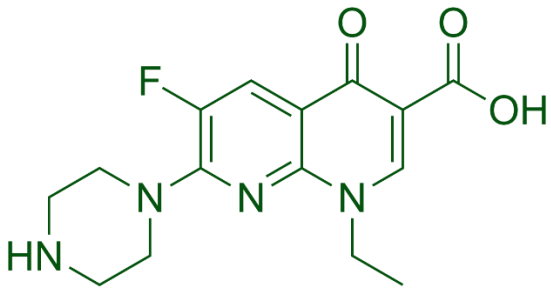
Side Effects

- GI disturbances, dizziness, headache.
- Tendon rupture (especially in elderly and corticosteroid users).
- QT prolongation, photosensitivity.

3. Enoxacin

Chemical Structure / Formula

- **Formula:** C15H17FN4O3
- **Structure:** A **fluorinated 4-quinolone** with enhanced **DNA gyrase inhibition**.



Mechanism of Action

- Inhibits bacterial DNA gyrase and topoisomerase IV, leading to double-strand DNA breaks.

Uses

- Treats UTIs, gonorrhea, prostatitis.
- Less commonly used due to the availability of newer fluoroquinolones.

Side Effects

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