

Indiana Medicaid Therapeutics Committee Therapeutic Class Review Summary

Therapeutic Class:

Fluoroquinolones

Overview:

The fluoroquinolones are synthetic, broad-spectrum antibacterial agents that inhibit DNA gyrase and topoisomerase IV. DNA gyrase is an essential enzyme that is involved in the replication, transcription and repair of bacterial DNA. Topoisomerase IV is an enzyme that plays a key role in the partitioning of the chromosomal DNA during bacterial cell division.

The broad category of fluoroquinolones refers to antibacterials characterized by the addition of a fluorine atom to the quinolone structure of drugs such as nalidixic acid and cinoxin. These two agents, though no longer available, are classified as first-generation quinolones. The second-generation quinolones, which are ciprofloxacin, lomefloxacin, norfloxacin, and ofloxacin, came to market in the mid 1980s. Compared to non-fluorinated quinolones, these agents have improved pharmacokinetics and increased gram-negative and systemic activity. Clinical uses include uncomplicated and complicated urinary tract infections (UTIs) and pyelonephritis, sexually transmitted diseases (STDs), prostatitis, and skin and soft tissue infections. Ciprofloxacin is the most potent fluoroquinolone against *Pseudomonas aeruginosa*. However, resistance to ciprofloxacin has developed in strains of *P. aeruginosa* and *Serratia marcescens*. Ciprofloxacin also has good penetration into bone, which makes it a useful alternative to parenteral antibiotics for the treatment of osteomyelitis caused by susceptible organisms. Ofloxacin is the most active second generation quinolone against *Chlamydia trachomatis*, and it exhibits the greatest activity of the group against *Staphylococcus aureus*. However, second generation fluoroquinolones should be used cautiously in treating this organism. Ciprofloxacin can be administered once daily in the form of an extended-release tablet (eg, Cipro[®] XR and ProQuin[®] XR).

The third generation quinolones include gatifloxacin, gemifloxacin, levofloxacin, moxifloxacin, and sparfloxacin. In May 2006, Bristol-Myers Squibb discontinued marketing of gatifloxacin worldwide due to its association with significant hyper/hypoglycemia. Levofloxacin is the levo- isomer and more active component of the ofloxacin racemic mixture. Third generation fluoroquinolones have extended activity against gram-positive pathogens, particularly penicillin-sensitive and penicillin-resistant *Streptococcus pneumoniae*, and atypical pathogens such as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*. Among all third generation quinolones, gemifloxacin and moxifloxacin have the lowest MIC (in vitro) against multi-drug resistant *Streptococcus pneumoniae*. Third generation agents also have broad gram-negative coverage but are less active than ciprofloxacin against *Pseudomonas* species. The long half-lives of gemifloxacin and moxifloxacin allow once daily dosing. Clinical uses of the third generation quinolones include community-acquired pneumonia, acute sinusitis, and acute exacerbations of chronic bronchitis. In addition, levofloxacin is indicated to treat UTIs, skin/structure infections, chronic bacterial prostatitis, and to prevent inhalation anthrax. Moxifloxacin is also indicated to treat both complicated and uncomplicated skin and skin structure infections.

Currently, ciprofloxacin, and ofloxacin are the only quinolones available as generics.



GENERIC NAME	TRADE NAME	MANUFACTURER	GENERIC
2 nd generation quinolones			
Ciprofloxacin	Cipro [®] , Cipro [®] XR, ProQuin [®] XR	Schering Corp (Cipro [®] , Cipro [®] XR), Esprit Pharma (ProQuin [®] XR), various	Y (Cipro [®] , Cipro [®] XR) N (ProQuin [®] XR)
Lomefloxacin	Maxaquin [®] (PRODUCT DISCONTINUED)	Pharmacia/Upjohn Div Pfizer	N
Norfloxacin	Noroxin [®]	Merck & Co., Inc.	N
Ofloxacin	Floxin [®]	Ortho-McNeil Pharmaceutical	Y
3 rd generation quinolones			
Gatifloxacin	Tequin [®] (PRODUCT DISCONTINUED)	Bristol-Myers Squibb	N
Gemifloxacin	Factive [®]	Oscient Pharmaceuticals	N
Levofloxacin	Levaquin [®]	Ortho-McNeil Pharmaceutical	N
Moxifloxacin	Avelox [®]	Schering Corp	N
Sparfloxacin	Zagam [®] (PRODUCT DISCONTINUED)	Bertek Pharmaceuticals	N

Summary:

The criteria for selection of an agent for the preferred drug list should include spectrum of activity, efficacy, cost, and safety.

