National Essential Medicine List Medication Review Process
Primary Healthcare
Component: Infections

Medication: Nalidixic acid

First generation (e.g. nalidixic acid) and second generation (e.g. ciprofloxacin) fluoroquinolones selectively inhibit bacterial DNA gyrase causing an inhibition of DNA synthesis. Third and fourth generation fluoroquinolones (e.g. moxifloxacin) are more selective for topoisomerase IV, which confers enhanced Gram positive coverage.

The major mechanism of resistance to quinolones occurs due to mutations in the target enzymes: DNA gyrase and topoisomerase IV.

Following first step mutations in DNA gyrasea reduction in susceptibility occurs. Additional mutations further augment resistance, thereby reducing drug affinity.

The rate of development of spontaneous first step resistance mutations in DNA gyrase occurs much more frequently following exposure to sub-inhibitory concentrations of nalidixic acid than to later generations of fluoroquinolones: 10^{-6} to 10^{-8}compared with$10^{-9}$to 10^{-10} (Chin et al). Mutations in DNA gyrase conferring resistance to nalidixic acid have been shown to also compromise the effect of later generation fluoroquinolones such as ciprofloxacin.

Nalidixic acid use is thus more likely to result in the development of resistance, which also affects later generations of fluoroquinolones.

Reference

Chin,N.X, Brittain,D.C, and Neu,H.C. In vitro activity activity of Ro 23-6240, a new fluorinated 4-quinolone. Antimicrob. Agents Chemother. 1986;29:675-680