Azithromycin, clarithromycin, erythromycin and roxithromycin have a wide spectrum of activity covering Gram-positive cocci, Legionella, Corynebacteria, Gram-negative cocci, Mycoplasma, Chlamydia and both Gram-positive and Gram-negative anaerobes but not enteric Gram-negative rods.

Erythromycin, azithromycin and clarithromycin are also active against Bordetella.

- Clarithromycin, unlike other macrolides, has a microbiologically active metabolite. It has activity against Mycobacterium avium complex (MAC) and is used in combination with other drugs for the treatment of this infection. It is also used in combination with other drugs in the eradication of Helicobacter pylori infection.

Azithromycin is less active than erythromycin against Gram-positive pathogens, but has activity against a few Gram-negative bacteria, some anaerobes, nontuberculous mycobacteria including MAC, and also against some parasites (eg Toxoplasma gondii).

The newer macrolides have more reliable absorption and longer half-lives (azithromycin > roxithromycin > clarithromycin > erythromycin) allowing less frequent dosing. They attain high intracellular concentrations that confer theoretical benefits in the treatment of infections due to intracellular pathogens.

- Erythromycin and clarithromycin are potent inhibitors of the cytochrome P450 (CYP3A4) enzyme system, so significant drug interactions occur. Co-administration of colchicine and clarithromycin or erythromycin has been associated with increased risk of fatal bone marrow toxicity. Erythromycin and clarithromycin have the potential to prolong the QT interval, with the other macrolides being associated with case reports.

The oral formulations of erythromycin have variable absorption and frequent gastrointestinal adverse effects. In babies less than one month old, erythromycin is generally not recommended because of concerns it may cause pyloric stenosis.