such as *Haemophilus influenzae* and *Moraxella catarrhalis* (*Branhamella catarrhalis*), as well as having activity against some of the Enterobacteriaceae such as *Escherichia coli and Salmonella* and *Shigella* spp.

Azithromycin is also more active than erythromycin against *Chlamydia trachomatis* and *Ureaplasma urealyticum*, and some opportunistic mycobacteria, including Mycobacterium avium complex. It has activity against the protozoa *Toxoplasma gondii* and *Plasmodium falciparum*.

Pharmacokinetics
Azithromycin given orally is rapidly absorbed and about 40% bioavailable. Absorption from capsules, but not tablets or suspension, is reduced by food. Peak plasma concentrations occur 2 to 3 hours after an oral dose and 1 to 2 hours after intravenous dosage. However, azithromycin is extensively distributed into the tissues, and tissue concentrations subsequently remain much higher than those in the blood; in contrast to most other antibacterials, plasma concentrations are therefore of little value as a guide to efficacy. High concentrations are taken up into white blood cells. There is little diffusion into the CSF when the meninges are not inflamed. Data from *animal* studies indicate that azithromycin crosses the placenta. Small amounts of azithromycin are demethylated in the liver, and it is excreted in bile mainly as unchanged drug and a number of inactive metabolites have also been detected. About 6% of an oral dose (representing about 20% of the amount in the systemic circulation) is excreted in the urine. The terminal elimination half-life is about 68 hours.

Indications:
It is given in the treatment of respiratory-tract infections (including otitis media), in skin and soft-tissue infections, and in uncomplicated genital infections. Azithromycin may also be used for the prophylaxis, and as a component of regimens in the treatment of *Mycobacterium avium complex* (MAC).

Dosage and Administration
The usual oral adult dose of azithromycin is 500 mg as a single dose daily for 3 days. For uncomplicated genital infections caused by *Chlamydia trachomatis* and for chancroid, 1 g of azithromycin is given as a single dose. A single dose of 2 g has been given for uncomplicated gonorrhoea. For the treatment of granuloma inguinale, an initial dose of 1 g followed by 500 mg daily may be given, or 1 g may be given once a week for at least 3 weeks, until all lesions have completely healed. For prophylaxis of disseminated MAC infections, azithromycin 1.2 g may be given once weekly. For mild or moderate typhoid caused by multi-drug resistant strains, 500 mg once daily may be given for 7days.

Drug Interactions
• Drugs Affecting or Metabolized by Hepatic Microsomal Enzymes

Many drug interactions reported in clinical trials with macrolides (e.g., erythromycin, clarithromycin) have not been reported to date with azithromycin. While azithromycin appears to have no effect on the cytochrome P-450 (CYP) enzyme system and interactions mediated by this enzyme system would not be expected to occur, it should be kept in mind that azithromycin and other macrolides have similar pharmacologic effects and the possibility that similar drug interactions may occur cannot be ruled out.

Macrolide antibiotics may inhibit metabolism of pimozide, resulting in increased plasma concentrations of unchanged drug. Because such alterations in pharmacokinetics of pimozide may be associated with prolongation of the QT and QTc interval, the manufacturer of pimozide states that concomitant administration of pimozide and azithromycin, clarithromycin, or erythromycin is contraindicated. Unlike some macrolides (i.e., erythromycin, clarithromycin), azithromycin does not appear to alter the metabolism of terfenadine (no longer commercially available in the US).

• Antacids

Giving azithromycin with antacids containing aluminium or magnesium salts can reduce the rate, but not the extent, of its absorption; azithromycin should be given at least 1 hour before or 2 hours after the antacid.

• Antilipemic Agents

Azithromycin states that concomitant use of atorvastatin and azithromycin results in only a modest effect on the pharmacokinetics of the antilipemic agent and that dosage adjustments are not necessary when azithromycin and atorvastatin are used concomitantly. However, in a patient receiving long-term therapy with lovastatin, administration of oral azithromycin (250 mg daily for 5 days) appeared to precipitate rhabdomyolysis. Rhabdomyolysis has occurred rarely in patients receiving lovastatin, and some evidence suggests that concomitant administration of erythromycin may increase the risk of this adverse effect. While the mechanism of this interaction remains to be determined, the risk of drug-induced rhabdomyolysis should be considered in patients receiving azithromycin, erythromycin, or clarithromycin concomitantly with lovastatin or another hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitor.

• Antimalarial Agent (Quinine)

There is in vitro evidence of additive to synergistic effects between azithromycin and quinine against *P. falciparum*, including multidrug-resistant strains.

• Antiretroviral Agents

HIV Protease Inhibitors (Nelfinavir)

In healthy adults receiving nelfinavir (750 mg 3 times daily), administration of a single 1.2-g oral dose of azithromycin at steady state resulted in a 15% decrease in the mean $AUC_{0–8}$ of nelfinavir and its M8 metabolite, but peak plasma concentrations of nelfinavir and its M8 metabolite were not affected. However, concomitant use of these drugs increases the peak plasma concentration and area under the concentration-time curve (AUC) of azithromycin by about twofold. Although dosage adjustments are not necessary when azithromycin and nelfinavir are used concomitantly, patients should be closely monitored for azithromycin adverse effects (e.g., hepatic enzyme abnormalities, hearing impairment).
• Cyclosporine

Although specific drug interaction studies have not been performed with azithromycin, concomitant use with other macrolides has resulted in increased cyclosporine concentrations. Therefore, the patient should be carefully monitored if azithromycin and cyclosporine are used concomitantly.

• Pimozide

Because concomitant use of pimozide and other macrolides (e.g., clarithromycin) has increased pimozide concentrations and is associated with a risk of prolonged QT interval and serious cardiovascular effects, thus concomitant use of pimozide and macrolides (including azithromycin) is contraindicated.

Adverse Effects and Precautions
Gastrointestinal disturbances are the most frequent adverse effect of azithromycin but are usually mild and less frequent than with erythromycin. Headache, somnolence, and taste disturbances may occur. Severe hypersensitivity reactions occur rarely but may be prolonged. Thrombocytopenia and mild transient neutropenia have been rarely reported in patients receiving azithromycin. Pain and inflammation may occur at the site of intravenous infusions particularly at high concentrations.

Azithromycin should be used with caution in patients with hepatic or renal impairment. Hepatic side effects have infrequently included transient elevations of liver function