Azithromycin for Injection, USP

**INDICATIONS AND USAGE**

Azithromycin has been shown to be active against most isolates of the following microorganisms, both in vitro and in clinical infections as described in Table 3.

**Special Populations**

There was no significant difference in the disposition of azithromycin between male and female subjects. No dosage adjustment is recommended.

**DOSAGE AND ADMINISTRATION**

Azithromycin is contraindicated in patients with a history of cholestatic jaundice/hepatic dysfunction associated with prior use of azithromycin.

**ADVERSE REACTIONS**

**Respiratory System**

The most frequently reported adverse events associated with azithromycin reported in clinical studies include: nasopharyngitis, diarrhea, cough, pharyngitis, vulvovaginal candidiasis, and abdominal pain.

**Skin**

The most frequently reported adverse events associated with azithromycin reported in clinical studies include: skin rash, urticaria, hypersensitivity skin reactions, pruritus, rash, and exanthema.

**Gastrointestinal System**

The most frequently reported adverse events associated with azithromycin reported in clinical studies include: abdominal pain, nausea, diarrhea, and vomiting.

**Sensory System**

The most frequently reported adverse events associated with azithromycin reported in clinical studies include: headache, dizziness, and vertigo.

**Laboratory Abnormalities**

The most frequently reported laboratory abnormalities associated with azithromycin reported in clinical studies include: increases in liver enzymes (including SGOT, SGPT, alkaline phosphatase, and total bilirubin), decreases in platelet counts, and increases in BUN, creatinine, and uric acid.

**Impedibody Abnormalities**

The most frequently reported abnormalities associated with azithromycin reported in clinical studies include: increased levels of hepatic enzymes, increased levels of total bilirubin, increased levels of BUN, creatinine, and uric acid.

**Other**

The most frequently reported adverse events associated with azithromycin reported in clinical studies include: increased levels of hepatic enzymes, increased levels of total bilirubin, increased levels of BUN, creatinine, and uric acid.

**Precautions**

Azithromycin may cause changes in stool consistency (diarrhea) in patients taking the drug. This effect is usually reversible upon discontinuation of the drug. In patients who experience diarrhea, the drug should be discontinued and appropriate treatment for the underlying cause of diarrhea initiated.

**Drug Interactions**

Azithromycin is excreted by renal mechanisms, and as such, renal dysfunction may affect drug elimination.
Teratogenic Effects. Pregnancy Category B: Impaired fertility due to azithromycin was found.

Laboratory Test Interactions:

Co-administration of nelfinavir at steady-state with a single oral dose of azithromycin resulted in increased azithromycin serum concentrations.

Drug Interactions:

Non-steroidal anti-inflammatory drugs (NSAIDs) may displace azithromycin from protein binding sites and may increase the risk for adverse effects of azithromycin.

Azithromycin therapy may increase hypothermic effects when given concurrently with ergot alkaloids, such as dihydroergotamine and ergotamine, and may enhance the toxic response to these drugs.

Cimetidine, omeprazole, clarithromycin and rifampin may affect azithromycin serum concentrations.

Warfarin: Concomitant administration of azithromycin and warfarin may result in increased anticoagulant effects; therefore, monitoring of INR should be closely conducted.

Co-administration of nelfinavir with azithromycin in healthy male volunteers resulted in increased azithromycin serum concentrations.

Drug interactions: Azithromycin may inhibit the hepatic drug metabolism and may increase the blood levels of the substrates of CYP3A4, CYP2C9, and CYP2C19, such as amiodarone, ergot derivatives, theophylline, midazolam, and Lovastatin. (See CLINICAL PHARMACOLOGY, Special Populations, Hepatic Insufficiency.)

Concurrent use of azithromycin and all products containing ergot alkaloids (e.g., ergotamine, dihydroergotamine, methylergometrine) may cause ergotism characterized by severe vasoconstriction, including hypertension, forearm and leg ischemia, prolonged uterine contraction, and maternal and fetal toxicity.

Terfenadine, cyclosporine, hexobarbital and phenytoin - elevated concentrations.

Ergotamine or dihydroergotamine - acute ergot toxicity characterized by severe peripheral vasospasm and dysesthesia.

Phospholipidosis: In male rats treated with azithromycin for 26 weeks, phospholipidosis was noted in some tissues including testes. This effect was dose dependent, and was seen in a similar incidence in male and female rats treated with azithromycin at doses equivalent to 10 times the maximum recommended human dose on a mg/m² basis.

C. difficile: To screen for C. difficile in patients taking prolonged courses of antibiotics, including azithromycin, stool should be sampled and tested for C. difficile for at least 2 weeks after therapy is completed.

Phospholipidosis (intracellular phospholipid accumulation) has been observed in some tissues of mice, rats, and dogs given multiple doses of azithromycin. In a 26-week study in male rats, phospholipidosis was noted in multiple tissues, including testes, and was dose related in the testes. It was also noted in the ovaries of female rats treated at doses equivalent to 10 times the maximum recommended human dose on a mg/m² basis. In a 104-week study in dogs treated with azithromycin at doses of 14 to 28 mg/kg/day, phospholipidosis was noted in the testes and epididymides of some males treated at the high dose level, and in the ovaries of an occasional female treated at all dose levels.

In the 104-week study, phospholipidosis was noted occasionally in some tissues of dogs treated at all dose levels of azithromycin, and was found in some tissues of dogs treated at lower dose levels. In most cases, the phospholipidosis was reversible after cessation of azithromycin treatment.

Azithromycin for injection is contraindicated in patients who are allergic to macrolide antibiotics or their products. Azithromycin is contraindicated in patients with known or suspected primary monomeric antibody deficiency. Azithromycin is also contraindicated in patients with a history of drug-induced lupus.

Administration should be avoided in patients with hepatic insufficiency due to azithromycin. Azithromycin is contraindicated in patients with impaired renal function treated with hemodialysis. When azithromycin is administered to patients with reduced renal function, it should be started with a reduced dose, the dose should be titrated based on pharmacokinetic parameters, and it should be used with caution in patients with hepatic insufficiency due to azithromycin.

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