AZITHROMYCIN- azithromycin tablet, film coated
Proficient Rx LP

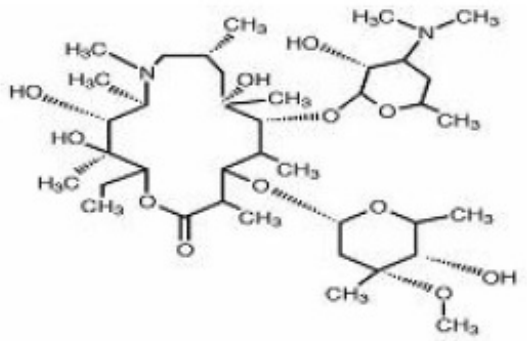
AZITHROMYCIN Tablets USP
250 mg and 500 mg

To reduce the development of drug-resistant bacteria and maintain the effectiveness of azithromycin tablets and other antibacterial drugs, azithromycin tablets should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

DESCRIPTION

Azithromycin tablets USP contain the active ingredient azithromycin, USP, an azalide, a subclass of macrolide antibiotics, for oral administration. Azithromycin, USP has the chemical name *(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)*-13-[(2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-α-*L*-*ribo*-hexopyranosyl) oxy]-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-11-[[3,4,6-trideoxy-3- (dimethylamino)-β-*D*-*xylo*-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadecan-15-one. Azithromycin, USP is derived from erythromycin; however, it differs chemically from erythromycin in that a methyl-substituted nitrogen atom is incorporated into the lactone ring.

Azithromycin, USP has the following structural formula:



$C_{38}H_{72}N_2O_{12}$ M.W. 749

Azithromycin, USP, as the monohydrate, is a white crystalline powder with a molecular formula of $C_{38}H_{72}N_2O_{12}•H_2O$ and a molecular weight of 767.

Azithromycin tablets USP are supplied for oral administration as tablets containing azithromycin monohydrate equivalent to either 250 mg or 500 mg azithromycin, USP and the following inactive ingredients: corn starch, dibasic calcium phosphate anhydrous, croscarmellose sodium, hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium citrate, sodium lauryl sulfate, and titanium dioxide.

The 500 mg tablets also contain FD&C blue #2.

CLINICAL PHARMACOLOGY

Pharmacokinetics

Following oral administration of a single 500 mg dose (two 250 mg tablets) to 36 fasted healthy male volunteers, the mean (SD) pharmacokinetic parameters were AUC_{0-72} = 4.3 (1.2) mcg·h/mL; C_{max} = 0.5 (0.2) mcg/mL; T_{max} = 2.2 (0.9) hours.

With a regimen of 500 mg (two 250 mg capsules*) on day 1, followed by 250 mg daily (one 250 mg capsule) on days 2 through 5, the pharmacokinetic parameters of azithromycin in plasma in healthy young adults (18 to 40 years of age) are portrayed in the chart below. C_{min} and C_{max} remained essentially unchanged from day 2 through day 5 of therapy.

Pharmacokinetic Parameters (Mean)	Total n = 12 Day 1	 Day 5
C_{max} (mcg/mL)	0.41	0.24
T_{max} (h)	2.5	3.2
AUC_{0-24} (mcg·h/mL)	2.6	2.1
C_{min} (mcg/mL)	0.05	0.05
Urinary Excret. (% dose)	4.5	6.5

*Azithromycin 250 mg tablets are bioequivalent to 250 mg capsules in the fasted state. Azithromycin 250 mg capsules are no longer commercially available.

In a two-way crossover study, 12 adult healthy volunteers (6 males, 6 females) received 1,500 mg of azithromycin administered in single daily doses over either 5 days (two 250 mg tablets on day 1, followed by one 250 mg tablet on days 2 to 5) or 3 days (500 mg per day for days 1 to 3). Due to limited serum samples on day 2 (3 day regimen) and days 2 to 4 (5 day regimen), the serum concentration-time profile of each subject was fit to a 3 compartment model and the $AUC_{0-\infty}$ for the fitted concentration profile was comparable between the 5 day and 3 day regimens.

	3 Day Regimen		5 Day Regimen	
Pharmacokinetic Parameter [mean (SD)]	Day 1	Day 3	Day 1	Day 5
C_{max} (serum, mcg/mL)	0.44 (0.22)	0.54 (0.25)	0.43 (0.20)	0.24 (0.06)
Serum $AUC_{0-\infty}$ (mcg·hr/mL)	17.4 (6.2)*		14.9 (3.1)*	
Serum $T_{1/2}$	71.8 hr		68.9 hr	

* Total AUC for the entire 3 day and 5 day regimens

Median azithromycin exposure (AUC_{0-288}) in mononuclear (MN) and polymorphonuclear (PMN) leukocytes following either the 5 day or 3 day regimen was more than a 1000 fold and 800 fold greater than in serum, respectively. Administration of the same total dose with either the 5 day or 3 day regimen may be expected to provide comparable concentrations of azithromycin within MN and PMN leukocytes.

Two azithromycin 250 mg tablets are bioequivalent to a single 500 mg tablet.

Absorption

The absolute bioavailability of azithromycin 250 mg capsules is 38%.

In a two-way crossover study in which 12 healthy subjects received a single 500 mg dose of azithromycin (two 250 mg tablets) with or without a high fat meal, food was shown to increase C_{max} by 23% but had no effect on AUC.

When azithromycin suspension was administered with food to 28 adult healthy male subjects, C_{max} increased by 56% and AUC was unchanged.

The AUC of azithromycin was unaffected by coadministration of an antacid containing aluminum and magnesium hydroxide with azithromycin capsules; however, the C_{max} was reduced by 24%. Administration of cimetidine (800 mg) two hours prior to azithromycin had no effect on azithromycin absorption.

Distribution

The serum protein binding of azithromycin is variable in the concentration range approximating human exposure, decreasing from 51% at 0.02 mcg/mL to 7% at 2 mcg/mL.

Following oral administration, azithromycin is widely distributed throughout the body with an apparent steady-state volume of distribution of 31.1 L/kg. Greater azithromycin concentrations in tissues than in plasma or serum were observed. High tissue concentrations should not be interpreted to be quantitatively related to clinical efficacy. The antimicrobial activity of azithromycin is pH related and appears to be reduced with decreasing pH. However, the extensive distribution of drug to tissues may be relevant to clinical activity.

Selected tissue (or fluid) concentration and tissue (or fluid) to plasma/serum concentration ratios are shown in the following table:

AZITHROMYCIN CONCENTRATIONS FOLLOWING A 500 mg DOSE (TWO 250 mg CAPSULES) IN ADULTS*

TISSUE OR FLUID	TIME AFTER DOSE (h)	TISSUE OR FLUID CONCENTRATION (mcg/g or mcg/mL)	CORRESPONDING PLASMA OR SERUM LEVEL (mcg/mL)	TISSUE (FLUID) PLASMA (SERUM) RATIO
SKIN	72 to 96	0.4	0.012	35
LUNG	72 to 96	4	0.012	> 100
SPUTUM†	2 to 4	1	0.64	2
SPUTUM‡	10 to 12	2.9	0.1	30
TONSIL§	9 to 18	4.5	0.03	> 100
TONSIL§	180	0.9	0.006	> 100
CERVIX¶	19	2.8	0.04	70

* Azithromycin tissue concentrations were originally determined using 250 mg capsules.
† Sample was obtained 2 to 4 hours after the first dose.
‡ Sample was obtained 10 to 12 hours after the first dose.
§ Dosing regimen of two doses of 250 mg each, separated by 12 hours.
¶ Sample was obtained 19 hours after a single 500 mg dose.

The extensive tissue distribution was confirmed by examination of additional tissues and

fluids (bone, ejaculum, prostate, ovary, uterus, salpinx, stomach, liver, and gallbladder). As there are no data from adequate and well-controlled studies of azithromycin treatment of infections in these additional body sites, the clinical importance of these tissue concentration data is unknown.

Following a regimen of 500 mg on the first day and 250 mg daily for 4 days, only very low concentrations were noted in cerebrospinal fluid (less than 0.01 mcg/mL) in the presence of non-inflamed meninges.

Metabolism

In vitro and *in vivo* studies to assess the metabolism of azithromycin have not been performed.

Elimination

Plasma concentrations of azithromycin following single 500 mg oral and i.v. doses declined in a polyphasic pattern with a mean apparent plasma clearance of 630 mL/min and terminal elimination half-life of 68 hours. The prolonged terminal half-life is thought to be due to extensive uptake and subsequent release of drug from tissues.

Biliary excretion of azithromycin, predominantly as unchanged drug, is a major route of elimination. Over the course of a week, approximately 6% of the administered dose appears as unchanged drug in urine.

Special Populations

Renal insufficiency

Azithromycin pharmacokinetics were investigated in 42 adults (21 to 85 years of age) with varying degrees of renal impairment. Following the oral administration of a single 1,000 mg dose of azithromycin, mean C_{max} and AUC_{0-120} increased by 5.1% and 4.2%, respectively in subjects with mild to moderate renal impairment (GFR 10 to 80 mL/min) compared to subjects with normal renal function (GFR > 80 mL/min). The mean C_{max} and AUC_{0-120} increased 61% and 35%, respectively in subjects with severe renal impairment (GFR < 10 mL/min) compared to subjects with normal renal function (GFR > 80 mL/min) (see **DOSAGE AND ADMINISTRATION**).

Hepatic insufficiency

The pharmacokinetics of azithromycin in subjects with hepatic impairment have not been established.

Gender

There are no significant differences in the disposition of azithromycin between male and female subjects. No dosage adjustment is recommended based on gender.

Geriatric patients

When studied in healthy elderly subjects aged 65 to 85 years, the pharmacokinetic parameters of azithromycin in elderly men were similar to those in young adults; however, in elderly women, although higher peak concentrations (increased by 30 to 50%) were observed, no significant accumulation occurred.

Pediatric patients

In two clinical studies, azithromycin for oral suspension was dosed at 10 mg/kg on day 1, followed by 5 mg/kg on days 2 through 5 to two groups of pediatric patients (aged 1 to 5 years and 5 to 15 years, respectively). The mean pharmacokinetic parameters on day 5 were C_{max}= 0.216 mcg/mL, T_{max} = 1.9 hours, and AUC_{0-24} = 1.822 mcg·hr/mL for the 1- to 5-year-old group and were C_{max} = 0.383 mcg/mL, T_{max} = 2.4 hours, and AUC_{0-24} = 3.109 mcg·hr/mL for the 5- to 15-year-old group.

Two clinical studies were conducted in 68 pediatric patients aged 3 to 16 years to determine the pharmacokinetics and safety of azithromycin for oral suspension. Azithromycin was administered following a low-fat breakfast.

The first study consisted of 35 pediatric patients treated with 20 mg/kg/day (maximum daily dose 500 mg) for 3 days of whom 34 patients were evaluated for pharmacokinetics.

In the second study, 33 pediatric patients received doses of 12 mg/kg/day (maximum daily dose 500 mg) for 5 days of whom 31 patients were evaluated for pharmacokinetics.

In both studies, azithromycin concentrations were determined over a 24 hour period following the last daily dose. Patients weighing above 25 kg in the 3 day study or 41.7 kg in the 5 day study received the maximum adult daily dose of 500 mg. Eleven patients (weighing 25 kg or less) in the first study and 17 patients (weighing 41.7 kg or less) in the second study received a total dose of 60 mg/kg. The following table shows pharmacokinetic data in the subset of pediatric patients who received a total dose of 60 mg/kg.

Pharmacokinetic Parameter [mean (SD)]	3 Day Regimen (20 mg/kg x 3 days)	5 Day Regimen (12 mg/kg x 5 days)
n	11	17
C_{max} (mcg/mL)	1.1 (0.4)	0.5 (0.4)
T_{max} (hr)	2.7 (1.9)	2.2 (0.8)
AUC_{0-24} (mcg·hr/mL)	7.9 (2.9)	3.9 (1.9)

The similarity of the overall exposure ($AUC_{0-\infty}$) between the 3 day and 5 day regimens in pediatric patients is unknown.

Single dose pharmacokinetics in pediatric patients given doses of 30 mg/kg have not been studied (see **DOSAGE AND ADMINISTRATION**).

Drug-Drug Interactions

Drug interaction studies were performed with azithromycin and other drugs likely to be coadministered. The effects of coadministration of azithromycin on the pharmacokinetics of other drugs are shown in **Table 1** and the effect of other drugs on the pharmacokinetics of azithromycin are shown in **Table 2**.

Coadministration of azithromycin at therapeutic doses had a modest effect on the pharmacokinetics of the drugs listed in **Table 1**. No dosage adjustment of drugs listed in **Table 1** is recommended when coadministered with azithromycin.

Coadministration of azithromycin with efavirenz or fluconazole had a modest effect on the pharmacokinetics of azithromycin. Nelfinavir significantly increased the C_{max} and AUC of azithromycin. No dosage adjustment of azithromycin is recommended when administered with drugs listed in **Table 2** (see **PRECAUTIONS, Drug Interactions**).

Table 1. Drug Interactions: Pharmacokinetic Parameters for Coadministered Drugs in the Presence of Azithromycin

Coadministered Drug	Dose of Coadministered Drug	Dose of Azithromycin	n	Ratio (with/without azithromycin) of Coadministered Drug Pharmacokinetic Parameters (90% CI); No Effect = 1	
				Mean C_{max}	Mean AUC
Atorvastatin	10 mg/day x 8 days	500 mg/day PO on days 6 to 8	12	0.83 (0.63 to 1.08)	1.01 (0.81 to 1.25)
Carbamazepine	200 mg/day x 2 days, then 200 mg BID x 18 days	500 mg/day PO for days 16 to 18	7	0.97 (0.88 to 1.06)	0.96 (0.88 to 1.06)
Cetirizine	20 mg/day x 11 days	500 mg PO on day 7, then 250 mg/day on days 8 to 11	14	1.03 (0.93 to 1.14)	1.02 (0.92 to 1.13)
Didanosine	200 mg PO BID x 21 days	1,200 mg/day PO on days 8 to 21	6	1.44 (0.85 to 2.43)	1.14 (0.83 to 1.57)
Efavirenz	400 mg/day x 7 days	600 mg PO on day 7	14	1.04*	0.95*
Fluconazole	200 mg PO single dose	1,200 mg PO single dose	18	1.04 (0.98 to 1.11)	1.01 (0.97 to 1.05)
Indinavir	800 mg TID x 5 days	1,200 mg PO on day 5	18	0.96 (0.86 to 1.08)	0.90 (0.81 to 1)
Midazolam	15 mg PO on day 3	500 mg/day PO x 3 days	12	1.27 (0.89 to 1.81)	1.26 (1.01 to 1.56)
Nelfinavir	750 mg TID x 11 days	1,200 mg PO on day 9	14	0.90 (0.81 to 1.01)	0.85 (0.78 to 0.93)
Rifabutin	300 mg/day x 10 days	500 mg PO on day 1, then 250 mg/day on days 2 to 10	6	See footnote below	NA
Sildenafil	100 mg on days 1 and 4	500 mg/day PO x 3 days	12	1.16 (0.86 to 1.57)	0.92 (0.75 to 1.12)
Theophylline	4 mg/kg IV on	500 mg PO	10	1.19	1.02

	days 1, 11, 25	on day 7, 250 mg/day on days 8 to 11		(1.02 to 1.40)	(0.86 to 1.22)
Theophylline	300 mg PO BID x 15 days	500 mg PO on day 6, then 250 mg/day on days 7 to 10	8	1.09 (0.92 to 1.29)	1.08 (0.89 to 1.31)
Triazolam	0.125 mg on day 2	500 mg PO on day 1, then 250 mg/day on day 2	12	1.06*	1.02*
Trimethoprim/ Sulfamethoxazole	160 mg/800 mg/day PO x 7 days	1,200 mg PO on day 7	12	0.85 (0.75 to 0.97)/ 0.90 (0.78 to 1.03)	0.87 (0.80 to 0.95)/ 0.96 (0.88 to 1.03)
Zidovudine	500 mg/day PO x 21 days	600 mg/day PO x 14 days	5	1.12 (0.42 to 3.02)	0.94 (0.52 to 1.70)
Zidovudine	500 mg/day PO x 21 days	1,200 mg/day PO x 14 days	4	1.31 (0.43 to 3.97)	1.30 (0.69 to 2.43)

NA - Not Available

* 90% Confidence interval not reported

Mean rifabutin concentrations one-half day after the last dose of rifabutin were 60 ng/mL when coadministered with azithromycin and 71 ng/mL when coadministered with placebo.

Table 2. Drug Interactions: Pharmacokinetic Parameters for Azithromycin in the Presence of Coadministered Drugs (see PRECAUTIONS, Drug Interactions).

Coadministered Drug	Dose of Coadministered Drug	Dose of Azithromycin	n	Ratio (with/without coadministered drug) of Azithromycin Pharmacokinetic Parameters (90% CI); No Effect = 1	
				Mean C_{max}	Mean AUC
Efavirenz	400 mg/day x 7 days	600 mg PO on day 7	14	1.22 (1.04 to 1.42)	0.92*
Fluconazole	200 mg PO single dose	1,200 mg PO single dose	18	0.82 (0.66 to 1.02)	1.07 (0.94 to 1.22)
Nelfinavir	750 mg TID x 11 days	1,200 mg PO on day 9	14	2.36 (1.77 to 3.15)	2.12 (1.80 to 2.50)
Rifabutin	300 mg/day x 10 days	500 mg PO on day 1,	6	See footnote below	NA

		then 250 mg/day on days 2 to 10			

NA – Not Available

* 90% Confidence interval not reported

Mean azithromycin concentrations one day after the last dose were 53 ng/mL when coadministered with 300 mg daily rifabutin and 49 ng/mL when coadministered with placebo.

Pharmacodynamics

Cardiac Electrophysiology

QTc interval prolongation was studied in a randomized, placebo-controlled parallel trial in 116 healthy subjects who received either chloroquine (1000 mg) alone or in combination with azithromycin (500 mg, 1000 mg, and 1500 mg once daily). Coadministration of azithromycin increased the QTc interval in a dose-and concentration-dependent manner. In comparison to chloroquine alone, the maximum mean (95% upper confidence bound) increases in QTcF were 5 (10) ms, 7 (12) ms and 9 (14) ms with the coadministration of 500 mg, 1000 mg and 1500 mg azithromycin, respectively.

Microbiology

Mechanism of Action

Azithromycin binds to the 23S rRNA of the bacterial 50S ribosomal subunit. It blocks protein synthesis by inhibiting the transpeptidation/translocation step of protein synthesis and by inhibiting the assembly of the 50S ribosomal subunit.

Azithromycin concentrates in phagocytes and fibroblasts as demonstrated by *in vitro* incubation techniques. The ratio of intracellular to extracellular concentration was > 30 after one hour incubation. *In vivo* studies suggest that concentration in phagocytes may contribute to drug distribution to inflamed tissues.

Mechanism of Resistance

The most frequently encountered mechanism of resistance to azithromycin is modification of the 23S rRNA at positions corresponding to A2058 and A2059 in the *Escherichia coli* numbering system. In addition to cross resistance with other macrolides (erythromycin and clarithromycin), ribosomal modification may determine resistance to other antibiotic classes (lincosamides and streptogramins B) that bind to overlapping ribosomal sites.

Azithromycin has been shown to be active against most isolates of the following bacteria, both *in vitro* and in clinical infections [see **INDICATIONS AND USAGE**].

Gram-positive bacteria

Staphylococcus aureus
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

Gram-negative bacteria

Haemophilus ducreyi
Haemophilus influenzae
Moraxella catarrhalis
Neisseria gonorrhoeae

"Other" bacteria

Chlamydophila pneumoniae
Chlamydia trachomatis
Mycoplasma pneumoniae

The following *in vitro* data are available, **but their clinical significance is unknown.**

At least 90% of the following bacteria exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the azithromycin susceptible breakpoint of ≤ 4 mcg/mL. However, safety and effectiveness of azithromycin in treating clinical infections due to these bacteria have not been established in adequate and well-controlled trials.

Gram-positive bacteria

Beta-hemolytic streptococci (Groups C, F, G)
Viridans group streptococci

Gram-negative bacteria

Bordetella pertussis

Anaerobic bacteria

Peptostreptococcus species
Prevotella bivia

"Other" bacteria

Ureaplasma urealyticum
Legionella pneumophila

Susceptibility Testing Methods

When available, the results of *in vitro* susceptibility test results for antimicrobial drugs used in resident hospitals should be provided to the physician as periodic reports which describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports may differ from susceptibility data obtained from outpatient use, but could aid the physician in selecting the most effective antimicrobial.

Dilution Techniques

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized procedure. Standardized procedures are based on a dilution method[1,2] (broth or agar) or equivalent with standardized inoculum concentration and standardized concentration of azithromycin powder. The MIC values should be interpreted according to criteria provided in **Table 3**.

Diffusion Techniques

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure[2,3] requires the use of standardized inoculum concentration. This procedure uses paper disks impregnated with 15 mcg azithromycin to test the susceptibility of bacteria to azithromycin. The disk diffusion interpretive criteria are provided in **Table 3**.

Table 3. Susceptibility Test Interpretive Criteria for Azithromycin Susceptibility Test Result Interpretive Criteria

	Minimum Inhibitory Concentrations (mcg/mL)			**Disk Diffusion (zone diameters in mm)**		
Pathogen						
	S	**I**	**R**	**S**	**I**	**R**
Haemophilus influenzae[a]	≤ 4	--	--	≥ 12	--	--
Staphylococcus aureus	≤ 2	4	≥ 8	≥ 18	14 to 17	≤ 13
Streptococci including *S. pneumoniae*	≤ 0.5	1	≥ 2	≥ 18	14 to 17	≤ 13

Susceptibility to azithromycin must be tested in ambient air.

[a]Insufficient information is available to determine Intermediate or Resistant interpretive criteria The ability to correlate MIC values and plasma drug levels is difficult as azithromycin concentrates in macrophages and tissues [see **Clinical Pharmacology**].

A report of “susceptible” indicates that the pathogen is likely to be inhibited if the antimicrobial compound reaches the concentrations usually achievable. A report of “intermediate” indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone which prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of “resistant” indicates that the pathogen is not likely to be inhibited if the antimicrobial compound reaches the concentrations usually achievable; other therapy should be selected.

Quality control

Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of supplies and reagents used in the assay, and the techniques of the individual performing the test. Standard azithromycin powder should provide the following range of MIC values noted in **Table 4**. For the diffusion technique using the azithromycin 15 mcg disk, the criteria in **Table 4** should be achieved.

Table 4. Acceptable Quality Control Ranges for Azithromycin

QC Strain	Minimum Inhibitory Concentrations (mcg/mL)	Disk Diffusion (zone diameters in mm)
Haemophilus influenzae ATCC* 49247	1 to 4	13 to 21
Staphylococcus aureus ATCC 29213	0.5 to 2	...
Staphylococcus aureus ATCC 25923	...	21 to 26
Streptococcus pneumoniae ATCC 49619	0.06 to 0.25	19 to 25

Susceptibility to azithromycin must be tested in ambient air.
*ATCC = American Type Culture Collection

INDICATIONS AND USAGE

Azithromycin tablets USP are indicated for the treatment of patients with mild to moderate infections (pneumonia: see WARNINGS) caused by susceptible strains of the designated microorganisms in the specific conditions listed below. As recommended dosages, durations of therapy and applicable patient populations vary among these infections, please see DOSAGE AND ADMINISTRATION for specific dosing recommendations.

Adults

Acute bacterial exacerbations of chronic obstructive pulmonary disease due to *Haemophilus influenzae, Moraxella catarrhalis* or *Streptococcus pneumoniae.*

Acute bacterial sinusitis due to *Haemophilus influenzae, Moraxella catarrhalis* or *Streptococcus pneumoniae*.

Community-acquired pneumonia due to *Chlamydophila pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae* or *Streptococcus pneumoniae* in patients appropriate for oral therapy.

NOTE: Azithromycin should not be used in patients with pneumonia who are judged to be inappropriate for oral therapy because of moderate to severe illness or risk factors such as any of the following:

patients with cystic fibrosis,
patients with nosocomially acquired infections,
patients with known or suspected bacteremia,
patients requiring hospitalization,
elderly or debilitated patients, or
patients with significant underlying health problems that may compromise their ability to respond to their illness (including immunodeficiency or functional asplenia).

Pharyngitis/tonsillitis caused by *Streptococcus pyogenes* as an alternative to first-line therapy in individuals who cannot use first-line therapy.

NOTE: Penicillin by the intramuscular route is the usual drug of choice in the

treatment of *Streptococcus pyogenes* infection and the prophylaxis of rheumatic fever. Azithromycin tablets USP are often effective in the eradication of susceptible strains of *Streptococcus pyogenes* from the nasopharynx. Because some strains are resistant to azithromycin tablets USP, susceptibility tests should be performed when patients are treated with azithromycin tablets USP. Data establishing efficacy of azithromycin in subsequent prevention of rheumatic fever are not available.

Uncomplicated skin and skin structure infections due to *Staphylococcus aureus, Streptococcus pyogenes,* or *Streptococcus agalactiae.* Abscesses usually require surgical drainage.

Urethritis and cervicitis due to *Chlamydia trachomatis* or *Neisseria gonorrhoeae*.

Genital ulcer disease in men due to *Haemophilus ducreyi* (chancroid). Due to the small number of women included in clinical trials, the efficacy of azithromycin in the treatment of chancroid in women has not been established.

Azithromycin tablets USP, at the recommended dose, should not be relied upon to treat syphilis. Antimicrobial agents used in high doses for short periods of time to treat non-gonococcal urethritis may mask or delay the symptoms of incubating syphilis. All patients with sexually-transmitted urethritis or cervicitis should have a serologic test for syphilis and appropriate cultures for gonorrhea performed at the time of diagnosis. Appropriate antimicrobial therapy and follow-up tests for these diseases should be initiated if infection is confirmed.

Appropriate culture and susceptibility tests should be performed before treatment to determine the causative organism and its susceptibility to azithromycin, USP. Therapy with azithromycin tablets USP may be initiated before results of these tests are known; once the results become available, antimicrobial therapy should be adjusted accordingly.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of azithromycin tablets USP and other antibacterial drugs, azithromycin tablets USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Pediatric Patients

(See **PRECAUTIONS, Pediatric Use** and **CLINICAL STUDIES, Pediatric Patients.)**

Acute otitis media caused by *Haemophilus influenzae, Moraxella catarrhalis,* or *Streptococcus pneumoniae.* (For specific dosage recommendation, see **DOSAGE AND ADMINISTRATION**.)

Community-acquired pneumonia due to *Chlamydophila pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae* or *Streptococcus pneumoniae* in patients appropriate for oral therapy. (For specific dosage recommendation, see **DOSAGE AND ADMINISTRATION**.)

NOTE: Azithromycin should not be used in pediatric patients with pneumonia who are judged to be inappropriate for oral therapy because of moderate to severe illness or risk factors such as any of the following:

patients with cystic fibrosis,
patients with nosocomially acquired infections,
patients with known or suspected bacteremia,
patients requiring hospitalization, or
patients with significant underlying health problems that may compromise their ability to respond to their illness (including immunodeficiency or functional asplenia).

Pharyngitis/tonsillitis caused by *Streptococcus pyogenes* as an alternative to first-line therapy in individuals who cannot use first-line therapy. (For specific dosage recommendation, see **DOSAGE AND ADMINISTRATION**.)

NOTE: Penicillin by the intramuscular route is the usual drug of choice in the treatment of *Streptococcus pyogenes* infection and the prophylaxis of rheumatic fever. Azithromycin tablets USP are often effective in the eradication of susceptible strains of *Streptococcus pyogenes* from the nasopharynx. Because some strains are resistant to azithromycin tablets USP, susceptibility tests should be performed when patients are treated with azithromycin tablets USP. Data establishing efficacy of azithromycin in subsequent prevention of rheumatic fever are not available.

Appropriate culture and susceptibility tests should be performed before treatment to determine the causative organism and its susceptibility to azithromycin. Therapy with azithromycin tablets USP may be initiated before results of these tests are known; once the results become available, antimicrobial therapy should be adjusted accordingly.

CONTRAINDICATIONS

Azithromycin is contraindicated in patients with known hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotic. Azithromycin is contraindicated in patients with a history of cholestatic jaundice/hepatic dysfunction associated with prior use of azithromycin.

WARNINGS

Hypersensitivity

Serious allergic reactions, including angioedema, anaphylaxis, and dermatologic reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported rarely in patients on azithromycin therapy. Although rare, fatalities have been reported (see **CONTRAINDICATIONS**). Despite initially successful symptomatic treatment of the allergic symptoms, when symptomatic therapy was discontinued, the allergic symptoms **recurred soon thereafter in some patients without further azithromycin exposure.** These patients required prolonged periods of observation and symptomatic treatment. The relationship of these episodes to the long tissue half-life of azithromycin and subsequent prolonged exposure to antigen is unknown at present.

If an allergic reaction occurs, the drug should be discontinued and appropriate therapy should be instituted. Physicians should be aware that reappearance of the allergic symptoms may occur when symptomatic therapy is discontinued.

Hepatotoxicity

Abnormal liver function, hepatitis, cholestatic jaundice, hepatic necrosis, and hepatic failure have been reported, some of which have resulted in death. Discontinue azithromycin immediately if signs and symptoms of hepatitis occur.

Treatment of Pneumonia

In the treatment of pneumonia, azithromycin has only been shown to be safe and effective in the treatment of community-acquired pneumonia due to *Chlamydia pneumoniae, Haemophilusinfluenzae, Mycoplasma pneumoniae* or *Streptococcus pneumoniae* in patients appropriate for oral therapy. Azithromycin should not be used in patients with pneumonia who are judged to be inappropriate for oral therapy because of moderate to severe illness or risk factors such as any of thefollowing: patients with cystic fibrosis, patients with nosocomially acquired infections, patients with known or suspected bacteremia, patients requiring hospitalization, elderly or debilitated patients, or patients with significant underlying health problems that may compromise their ability to respond totheir illness (including immunodeficiency or functional asplenia).

***Clostridium Difficile*-Associated Diarrhea**

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including azithromycin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

QT Prolongation

Prolonged cardiac repolarization and QT interval, imparting a risk of developing cardiac arrhythmia and torsade de pointes, have been seen in treatment with macrolides, including azithromycin. Cases of torsade de pointes have been spontaneously reported during postmarketing surveillance in patients receiving azithromycin. Providers should consider the risk of QT prolongation which can be fatal when weighing the risks and benefits of azithromycin for at-risk groups including:

- patients with known prolongation of the QT interval, a history of torsade de pointes, congenital long QT syndrome, bradyarrhythmias or uncompensated heart failure
- patients on drugs known to prolong the QT interval
- patients with ongoing proarrhythmic conditions such as uncorrected hypokalemia or hypomagnesemia, clinically significant bradycardia, and in patients receiving

Class IA (quinidine, procainamide) or Class III (dofetilide, amiodarone, sotalol) antiarrhythmic agents.

Elderly patients may be more susceptible to drug-associated effects on the QT interval.

PRECAUTIONS

General

Because azithromycin is principally eliminated via the liver, caution should be exercised when azithromycin is administered to patients with impaired hepatic function. Due to the limited data in subjects with GFR < 10 mL/min, caution should be exercised when prescribing azithromycin in these patients (see **CLINICAL PHARMACOLOGY, Special Populations,** *Renal insufficiency*).

Exacerbation of symptoms of myasthenia gravis and new onset of myasthenic syndrome have been reported in patients receiving azithromycin therapy.

Prescribing azithromycin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients

Azithromycin tablets can be taken with or without food.

Patients should also be cautioned not to take aluminum- and magnesium-containing antacids and azithromycin simultaneously.

The patient should be directed to discontinue azithromycin immediately and contact a physician if any signs of an allergic reaction occur.

Patients should be counseled that antibacterial drugs including azithromycin tablets should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When azithromycin tablets are prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of the therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by azithromycin tablets or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Drug Interactions

Coadministration of nelfinavir at steady-state with a single oral dose of azithromycin resulted in increased azithromycin serum concentrations. Although a dose adjustment of azithromycin is not recommended when administered in combination with nelfinavir, close monitoring for known side effects of azithromycin, such as liver enzyme

abnormalities and hearing impairment, is warranted (see **ADVERSE REACTIONS**).

Although, in a study of 22 healthy men, a 5 day course of azithromycin did not affect the prothrombin time from a subsequently administered dose of warfarin, spontaneous postmarketing reports suggest that concomitant administration of azithromycin may potentiate the effects of oral anticoagulants. Prothrombin times should be carefully monitored while patients are receiving azithromycin and oral anticoagulants concomitantly.

Drug interaction studies were performed with azithromycin and other drugs likely to be coadministered (see **CLINICAL PHARMACOLOGY, Drug-Drug Interactions**). When used in therapeutic doses, azithromycin had a modest effect on the pharmacokinetics of atorvastatin, carbamazepine, cetirizine, didanosine, efavirenz, fluconazole, indinavir, midazolam, rifabutin, sildenafil, theophylline (intravenous and oral), triazolam, trimethoprim/sulfamethoxazole or zidovudine. Coadministration with efavirenz or fluconazole had a modest effect on the pharmacokinetics of azithromycin. No dosage adjustment of either drug is recommended when azithromycin is coadministered with any of the above agents.

Interactions with the drugs listed below have not been reported in clinical trials with azithromycin; however, no specific drug interaction studies have been performed to evaluate potential drug-drug interaction. Nonetheless, they have been observed with macrolide products. Until further data are developed regarding drug interactions when azithromycin and these drugs are used concomitantly, careful monitoring of patients is advised:

Digoxin–elevated digoxin concentrations.

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

Terfenadine, cyclosporine, hexobarbital and phenytoin concentrations.

Laboratory Test Interactions

There are no reported laboratory test interactions.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate carcinogenic potential. Azithromycin has shown no mutagenic potential in standard laboratory tests: mouse lymphoma assay, human lymphocyte clastogenic assay, and mouse bone marrow clastogenic assay. No evidence of impaired fertility due to azithromycin was found.

Pregnancy

Teratogenic Effects

Pregnancy Category B

Reproduction studies have been performed in rats and mice at doses up to moderately maternally toxic dose concentrations (i.e., 200 mg/kg/day). These doses, based on a mg/m^2 basis, are estimated to be 4 and 2 times, respectively, the human daily dose of

500 mg. In the animal studies, no evidence of harm to the fetus due to azithromycin was found. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, azithromycin should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether azithromycin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when azithromycin is administered to a nursing woman.

Pediatric Use

(See **CLINICAL PHARMACOLOGY, INDICATIONS AND USAGE,** and **DOSAGE AND ADMINISTRATION.)**

Acute Otitis Media (total dosage regimen: 30 mg/kg, see **DOSAGE AND ADMINISTRATION**): Safety and effectiveness in the treatment of pediatric patients with otitis media under 6 months of age have not been established.

Acute Bacterial Sinusitis (dosage regimen: 10 mg/kg on Days 1 to 3): Safety and effectiveness in the treatment of pediatric patients with acute bacterial sinusitis under 6 months of age have not been established. Use of azithromycin for the treatment of acute bacterial sinusitis in pediatric patients (6 months of age or greater) is supported by adequate and well-controlled studies in adults, similar pathophysiology of acute sinusitis in adults and pediatric patients, and studies of acute otitis media in pediatric patients.

Community-Acquired Pneumonia (dosage regimen: 10 mg/kg on Day 1 followed by 5 mg/kg on Days 2 to 5): Safety and effectiveness in the treatment of pediatric patients with community-acquired pneumonia under 6 months of age have not been established. Safety and effectiveness for pneumonia due to *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae* were documented in pediatric clinical trials. Safety and effectiveness for pneumonia due to *Haemophilus influenzae* and *Streptococcus pneumoniae* were not documented bacteriologically in the pediatric clinical trial due to difficulty in obtaining specimens. Use of azithromycin for these two microorganisms is supported, however, by evidence from adequate and well-controlled studies in adults.

Pharyngitis/Tonsillitis (dosage regimen: 12 mg/kg on Days 1 to 5): Safety and effectiveness in the treatment of pediatric patients with pharyngitis/tonsillitis under 2 years of age have not been established.

Studies evaluating the use of repeated courses of therapy have not been conducted (see **CLINICAL PHARMACOLOGY** and **ANIMAL TOXICOLOGY**).

Geriatric Use

Pharmacokinetic parameters in older volunteers (65 to 85 years old) were similar to those in younger volunteers (18 to 40 years old) for the 5 day therapeutic regimen. Dosage adjustment does not appear to be necessary for older patients with normal renal and hepatic function receiving treatment with this dosage regimen (see **CLINICAL PHARMACOLOGY**).

In multiple-dose clinical trials of oral azithromycin, 9% of patients were at least 65 years

of age (458/4949) and 3% of patients (144/4949) were at least 75 years of age. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in response between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Elderly patients may be more susceptible to development of torsade de pointes arrhythmia than younger patients (see **WARNINGS**).

Azithromycin tablets USP, 250 mg contain 0.36 mg of sodium per tablet.

Azithromycin tablets USP, 500 mg contain 0.73 mg of sodium per tablet.

ADVERSE REACTIONS

In clinical trials, most of the reported side effects were mild to moderate in severity and were reversible upon discontinuation of the drug. Potentially serious side effects of angioedema and cholestatic jaundice were reported rarely. Approximately 0.7% of the patients (adults and pediatric patients) from the 5 day multiple-dose clinical trials discontinued azithromycin therapy because of treatment-related side effects. In adults given 500 mg/day for 3 days, the discontinuation rate due to treatment-related side effects was 0.6%. In clinical trials in pediatric patients given 30 mg/kg, either as a single dose or over 3 days, discontinuation from the trials due to treatment-related side effects was approximately 1% (see **DOSAGE AND ADMINISTRATION**). Most of the side effects leading to discontinuation were related to the gastrointestinal tract, e.g., nausea, vomiting, diarrhea, or abdominal pain (see **CLINICAL STUDIES, Pediatric Patients**).

Clinical

Adults

Multiple-dose regimens

Overall, the most common treatment-related side effects in adult patients receiving multiple-dose regimens of azithromycin were related to the gastrointestinal system with diarrhea/loose stools (4 to 5%), nausea (3%) and abdominal pain (2 to 3%) being the most frequently reported.

No other treatment-related side effects occurred in patients on the multiple-dose regimens of azithromycin with a frequency greater than 1%. Side effects that occurred with a frequency of 1% or less included the following:

Cardiovascular: Palpitations, chest pain.

Gastrointestinal: Dyspepsia, flatulence, vomiting, melena and cholestatic jaundice.

Genitourinary: Monilia, vaginitis and nephritis.

Nervous System: Dizziness, headache, vertigo and somnolence.

General: Fatigue.

Allergic: Rash, pruritus, photosensitivity and angioedema.

Single 1 gram dose regimen

Overall, the most common side effects in patients receiving a single-dose regimen of 1 gram of azithromycin were related to the gastrointestinal system and were more frequently reported than in patients receiving the multiple-dose regimen.

Side effects that occurred in patients on the single one-gram dosing regimen of azithromycin with a frequency of 1% or greater included diarrhea/loose stools (7%), nausea (5%), abdominal pain (5%), vomiting (2%), dyspepsia (1%) and vaginitis (1%).

Single 2 gram dose regimen

Overall, the most common side effects in patients receiving a single 2 gram dose of azithromycin were related to the gastrointestinal system. Side effects that occurred in patients in this study with a frequency of 1% or greater included nausea (18%), diarrhea/loose stools (14%), vomiting (7%), abdominal pain (7%), vaginitis (2%), dyspepsia (1%) and dizziness (1%). The majority of these complaints were mild in nature.

Pediatric Patients

Single and multiple-dose regimens

The types of side effects in pediatric patients were comparable to those seen in adults, with different incidence rates for the dosage regimens recommended in pediatric patients.

Acute otitis media

For the recommended total dosage regimen of 30 mg/kg, the most frequent side effects (≥ 1%) attributed to treatment were diarrhea, abdominal pain, vomiting, nausea and rash (see **DOSAGE AND ADMINISTRATION** and **CLINICAL STUDIES, Pediatric Patients**).

The incidence, based on dosing regimen, is described in the table below:

Dosage Regimen	Diarrhea, %	Abdominal Pain, %	Vomiting, %	Nausea, %	Rash, %
1 day	4.3%	1.4%	4.9%	1%	1%
3 day	2.6%	1.7%	2.3%	0.4%	0.6%
5 day	1.8%	1.2%	1.1%	0.5%	0.4%

Community-acquired pneumonia

For the recommended dosage regimen of 10 mg/kg on Day 1 followed by 5 mg/kg on Days 2 to 5, the most frequent side effects attributed to treatment were diarrhea/loose stools, abdominal pain, vomiting, nausea and rash.

The incidence is described in the table below:

Dosage Regimen	Diarrhea/Loose stools, %	Abdominal Pain, %	Vomiting, %	Nausea, %	Rash, %
5 day	5.8%	1.9%	1.9%	1.9%	1.6%

Pharyngitis/tonsillitis

For the recommended dosage regimen of 12 mg/kg on Days 1 to 5, the most frequent side effects attributed to treatment were diarrhea, vomiting, abdominal pain, nausea and headache.

The incidence is described in the table below:

Dosage Regimen	Diarrhea, %	Abdominal Pain, %	Vomiting, %	Nausea, %	Rash, %	Headache, %
5 day	5.4%	3.4%	5.6%	1.8%	0.7%	1.1%

With any of the treatment regimens, no other treatment-related side effects occurred in pediatric patients treated with azithromycin with a frequency greater than 1%. Side effects that occurred with a frequency of 1% or less included the following:

Cardiovascular: Chest pain.

Gastrointestinal: Dyspepsia, constipation, anorexia, enteritis, flatulence, gastritis, jaundice, loose stools and oral moniliasis.

Hematologic and Lymphatic: Anemia and leukopenia.

Nervous System: Headache (otitis media dosage), hyperkinesia, dizziness, agitation, nervousness and insomnia.

General: Fever, face edema, fatigue, fungal infection, malaise and pain.

Allergic: Rash and allergic reaction.

Respiratory: Cough increased, pharyngitis, pleural effusion and rhinitis.

Skin and Appendages: Eczema, fungal dermatitis, pruritus, sweating, urticaria and vesiculobullous rash.

Special Senses: Conjunctivitis.

Postmarketing Experience

Adverse events reported with azithromycin during the postmarketing period in adult and/or pediatric patients for which a causal relationship may not be established include:

Allergic: Arthralgia, edema, urticaria and angioedema.

Cardiovascular: Arrhythmias including ventricular tachycardia and hypotension. There have been rare reports of QT prolongation and *torsade de pointes*.

Gastrointestinal: Anorexia, constipation, dyspepsia, flatulence, vomiting/diarrhea rarely resulting in dehydration, pseudomembranous colitis, pancreatitis, oral candidiasis, pyloric stenosis, and rare reports of tongue discoloration.

General: Asthenia, paresthesia, fatigue, malaise and anaphylaxis (rarely fatal).

Genitourinary: Interstitial nephritis and acute renal failure and vaginitis.

Hematopoietic: Thrombocytopenia.

Liver/Biliary: Adverse reactions related to hepatic dysfunction have been reported in

postmarketing experience with azithromycin (see **WARNINGS**, **Hepatotoxicity**).

Nervous System: Convulsions, dizziness/vertigo, headache, somnolence, hyperactivity, nervousness, agitation and syncope.

Psychiatric: Aggressive reaction and anxiety.

Skin/Appendages: Pruritus, rarely serious skin reactions including erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis.

Special Senses: Hearing disturbances including hearing loss, deafness and/or tinnitus and reports of taste/smell perversion and/or loss.

Laboratory Abnormalities

Adults

Clinically significant abnormalities (irrespective of drug relationship) occurring during the clinical trials were reported as follows: with an incidence of greater than 1%: decreased hemoglobin, hematocrit, lymphocytes, neutrophils and blood glucose; elevated serum creatine phosphokinase, potassium, ALT, GGT, AST, BUN, creatinine, blood glucose, platelet count, lymphocytes, neutrophils and eosinophils; with an incidence of less than 1%: leukopenia, neutropenia, decreased sodium, potassium, platelet count, elevated monocytes, basophils, bicarbonate, serum alkaline phosphatase, bilirubin, LDH and phosphate. The majority of subjects with elevated serum creatinine also had abnormal values at baseline.

When follow-up was provided, changes in laboratory tests appeared to be reversible.

In multiple-dose clinical trials involving more than 5000 patients, four patients discontinued therapy because of treatment-related liver enzyme abnormalities and one because of a renal function abnormality.

Pediatric Patients

One, three and five day regimens

Laboratory data collected from comparative clinical trials employing two 3 day regimens (30 mg/kg or 60 mg/kg in divided doses over 3 days), or two 5 day regimens (30 mg/kg or 60 mg/kg in divided doses over 5 days) were similar for regimens of azithromycin and all comparators combined, with most clinically significant laboratory abnormalities occurring at incidences of 1 to 5%. Laboratory data for patients receiving 30 mg/kg as a single dose were collected in one single center trial. In that trial, an absolute neutrophil count between 500 to 1500 cells/mm^3 was observed in 10/64 patients receiving 30 mg/kg as a single dose, 9/62 patients receiving 30 mg/kg given over 3 days, and 8/63 comparator patients. No patient had an absolute neutrophil count < 500 cells/mm^3 (see **DOSAGE AND ADMINISTRATION**).

In multiple-dose clinical trials involving approximately 4700 pediatric patients, no patients discontinued therapy because of treatment-related laboratory abnormalities.

DOSAGE AND ADMINISTRATION

(See **INDICATIONS AND USAGE** and **CLINICAL PHARMACOLOGY**.)

Adults

Infection*	Recommended Dose/Duration of Therapy
Community-acquired pneumonia (mild severity) Pharyngitis/tonsillitis (second line therapy) Skin/skin structure (uncomplicated)	500 mg as a single dose on Day 1, followed by 250 mg once daily on Days 2 through 5.
Acute bacterial exacerbations of chronic obstructive pulmonary disease (mild to moderate)	500 mg QD x 3 days OR 500 mg as a single dose on Day 1, followed by 250 mg once daily on Days 2 through 5.
Acute bacterial sinusitis	500 mg QD x 3 days
Genital ulcer disease (chancroid)	One single 1 gram dose
Non-gonococcal urethritis and cervicitis	One single 1 gram dose
Gonococcal urethritis and cervicitis	One single 2 gram dose

***DUE TO THE INDICATED ORGANISMS** (see**INDICATIONS AND USAGE**).

Azithromycin tablets USP can be taken with or without food.

Renal Insufficiency

No dosage adjustment is recommended for subjects with renal impairment (GFR ≤ 80 mL/min). The mean $AUC_{0\text{-}120}$ was similar in subjects with GFR 10 to 80 mL/min compared to subjects with normal renal function, whereas it increased 35% in subjects with GFR < 10 mL/min compared to subjects with normal renal function. Caution should be exercised when azithromycin is administered to subjects with severe renal impairment (see **CLINICAL PHARMACOLOGY, Special Populations,** *Renal insufficiency*).

Hepatic Insufficiency

The pharmacokinetics of azithromycin in subjects with hepatic impairment have not been established. No dose adjustment recommendations can be made in patients with impaired hepatic function (see **CLINICAL PHARMACOLOGY**, **Special Populations**, *Hepatic insufficiency*).

No dosage adjustment is recommended based on age or gender (see **CLINICAL PHARMACOLOGY**, **Special Populations**).

Pediatric Patients

Azithromycin for oral suspension can be taken with or without food.

Acute Otitis Media

The recommended dose of azithromycin for oral suspension for the treatment of pediatric patients with acute otitis media is 30 mg/kg given as a single dose or 10 mg/kg once daily for 3 days or 10 mg/kg as a single dose on the first day followed by 5

mg/kg/day on Days 2 through 5 (see chart below).

Acute Bacterial Sinusitis

The recommended dose of azithromycin for oral suspension for the treatment of pediatric patients with acute bacterial sinusitis is 10 mg/kg once daily for 3 days (see chart below).

Community-Acquired Pneumonia

The recommended dose of azithromycin for oral suspension for the treatment of pediatric patients with community-acquired pneumonia is 10 mg/kg as a single dose on the first day followed by 5 mg/kg on Days 2 through 5 (see chart below).

PEDIATRIC DOSAGE GUIDELINES FOR OTITIS MEDIA, ACUTE BACTERIAL SINUSITIS AND COMMUNITY-ACQUIRED PNEUMONIA
(Age 6 Months and Above, see PRECAUTIONS, Pediatric Use.)
Based on Body Weight

OTITIS MEDIA AND COMMUNITY-ACQUIRED PNEUMONIA: (5 Day Regimen)*							
Dosing Calculated on 10 mg/kg/day Day 1and 5 mg/kg/day Days 2 to 5.							
Weight		**100 mg/5 mL**		**200 mg/5 mL**		**Total mL perTreatmentCourse**	**Total mg perTreatmentCourse**
Kg	**Lbs.**	**Day 1**	**Days 2 to 5**	**Day 1**	**Days 2 to 5**		
5	11	2.5 mL (½ tsp)	1.25 mL (¼ tsp)			7.5 mL	150 mg
10	22	5 mL (1 tsp)	2.5 mL (½ tsp)			15 mL	300 mg
20	44			5 mL (1 tsp)	2.5 mL (½ tsp)	15 mL	600 mg
30	66			7.5 mL (1½ tsp)	3.75 mL (¾ tsp)	22.5 mL	900 mg
40	88			10 mL (2 tsp)	5 mL (1 tsp)	30 mL	1200 mg
50 and above	110 and above			12.5 mL (2½ tsp)	6.25 mL (1¼ tsp)	37.5 mL	1500 mg

* Effectiveness of the 3 day or 1 day regimen in pediatric patients with community-

acquired pneumonia has not been established.

OTITIS MEDIA AND ACUTE BACTERIAL SINUSITIS: (3 Day Regimen)*					
Dosing Calculated on 10 mg/kg/day					
Weight		100 mg/5 mL	200 mg/5 mL	Total mL perTreatmentCourse	Total mg perTreatmentCourse
Kg	Lbs.	Day 1 to 3	Day 1 to 3		
5	11	2.5 mL (½ tsp)		7.5 mL	150 mg
10	22	5 mL (1 tsp)		15 mL	300 mg
20	44		5 mL (1 tsp)	15 mL	600 mg
30	66		7.5 mL (1 ½ tsp)	22.5 mL	900 mg
40	88		10 mL (2 tsp)	30 mL	1200 mg
50 and above	110 and above		12.5 mL (2 ½ tsp)	37.5 mL	1500 mg

* Effectiveness of the 5 day or 1 day regimen in pediatric patients with acute bacterial sinusitis has not been established.

OTITIS MEDIA: (1 Day Regimen)				
Dosing Calculated on 30 mg/kg as a single dose				
Weight		200 mg/5 mL	Total mL perTreatment Course	Total mg perTreatment Course
Kg	Lbs.	Day 1		
5	11	3.75 mL (3/4 tsp)	3.75 mL	150 mg
10	22	7.5 mL (1 ½ tsp)	7.5 mL	300 mg
20	44	15 mL (3 tsp)	15 mL	600 mg
30	66	22.5 mL (4 ½ tsp)	22.5 mL	900 mg
40	88	30 mL (6 tsp)	30 mL	1200 mg
50 and above	110 and above	37.5 mL (7 ½ tsp)	37.5 mL	1500 mg

The safety of re-dosing azithromycin in pediatric patients who vomit after receiving 30 mg/kg as a single dose has not been established. In clinical studies involving 487 patients with acute otitis media given a single 30 mg/kg dose of azithromycin, eight patients who vomited within 30 minutes of dosing were re-dosed at the same total dose.

Pharyngitis/Tonsillitis

The recommended dose of azithromycin for children with pharyngitis/tonsillitis is 12 mg/kg once daily for 5 days (see chart below).

PEDIATRIC DOSAGE GUIDELINES FOR PHARYNGITIS/TONSILLITIS
(Age 2 Years and Above, see PRECAUTIONS, Pediatric Use.)
Based on Body Weight

PHARYNGITIS/TONSILLITIS: (5 Day Regimen)				
Dosing Calculated on 12 mg/kg/day for 5 days.				
Weight		**200 mg/5 mL**	**Total mL per TreatmentCourse**	**Total mg per TreatmentCourse**
Kg	**Lbs.**	**Day 1 to 5**		
8	18	2.5 mL (½ tsp)	12.5 mL	500 mg
17	37	5 mL (1 tsp)	25 mL	1000 mg
25	55	7.5 mL (1½ tsp)	37.5 mL	1500 mg
33	73	10 mL (2 tsp)	50 mL	2000 mg
40	88	12.5 mL (2½ tsp)	62.5 mL	2500 mg

HOW SUPPLIED

Azithromycin tablets USP, 250 mg are supplied as white, oval, biconvex, unscored, film-coated tablets, debossed with “787” on one side and “PLIVA” on the other, containing azithromycin monohydrate equivalent to 250 mg of azithromycin, USP, available in bottles of 4 tablets (NDC 63187-007-04) and boxes of 1 card x 6 tablets (NDC 63187-007-06).

Azithromycin tablets USP, 500 mg are supplied as blue, capsule shaped, biconvex, unscored, film-coated tablets, debossed with “788” on one side and “PLIVA” on the other, containing azithromycin monohydrate equivalent to 500 mg of azithromycin, USP, available in boxes of 1 card x 3 tablets (NDC 63187-189-03) and bottles of 4 tablets (NDC 63187-189-04).

Store at 20º to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

CLINICAL STUDIES

(See INDICATIONS AND USAGE and Pediatric Use.)

Pediatric Patients

From the perspective of evaluating pediatric clinical trials, Days 11 to 14 were considered on-therapy evaluations because of the extended half-life of azithromycin. Day 11 to 14 data are provided for clinical guidance. Day 24 to 32 evaluations were considered the primary test of cure endpoint.

Acute Otitis Media

Safety and efficacy using azithromycin 30 mg/kg given over 5 days

Protocol 1

In a double-blind, controlled clinical study of acute otitis media performed in the United States, azithromycin (10 mg/kg on Day 1 followed by 5 mg/kg on Days 2 to 5) was compared to amoxicillin/clavulanate potassium (4:1). For the 553 patients who were evaluated for clinical efficacy, the clinical success rate (i.e., cure plus improvement) at the Day 11 visit was 88% for azithromycin and 88% for the control agent. For the 521 patients who were evaluated at the Day 30 visit, the clinical success rate was 73% for azithromycin and 71% for the control agent.

In the safety analysis of the above study, the incidence of treatment-related adverse events, primarily gastrointestinal, in all patients treated was 9% with azithromycin and 31% with the control agent. The most common side effects were diarrhea/loose stools (4% azithromycin vs. 20% control), vomiting (2% azithromycin vs. 7% control), and abdominal pain (2% azithromycin vs. 5% control).

Protocol 2

In a non-comparative clinical and microbiologic trial performed in the United States, where significant rates of beta-lactamase producing organisms (35%) were found, 131 patients were evaluable for clinical efficacy. The combined clinical success rate (i.e., cure and improvement) at the Day 11 visit was 84% for azithromycin. For the 122 patients who were evaluated at the Day 30 visit, the clinical success rate was 70% for azithromycin.

Microbiologic determinations were made at the pre-treatment visit. Microbiology was not reassessed at later visits. The following presumptive bacterial/clinical cure outcomes (i.e., clinical success) were obtained from the evaluable group:

Presumed Bacteriologic Eradication

	Day 11 Azithromycin	Day 30 Azithromycin
S. pneumoniae	61/74 (82%)	40/56 (71%)
H. influenzae	43/54 (80%)	30/47 (64%)
M. catarrhalis	28/35 (80%)	19/26 (73%)
S. pyogenes	11/11 (100%)	7/7
Overall	177/217 (82%)	97/137 (73%)

In the safety analysis of this study, the incidence of treatment-related adverse events, primarily gastrointestinal, in all patients treated was 9%. The most common side effect was diarrhea (4%).

Protocol 3

In another controlled comparative clinical and microbiologic study of otitis media performed in the United States, azithromycin was compared to amoxicillin/clavulanate potassium (4:1). This study utilized two of the same investigators as Protocol 2 (above), and these two investigators enrolled 90% of the patients in Protocol 3. For this reason, Protocol 3 was not considered to be an independent study. Significant rates of beta-lactamase producing organisms (20%) were found. Ninety-two (92) patients were evaluable for clinical and microbiologic efficacy. The combined clinical success rate (i.e., cure and improvement) of those patients with a baseline pathogen at the Day 11 visit was 88% for azithromycin vs. 100% for control; at the Day 30 visit, the clinical success rate was 82% for azithromycin vs. 80% for control.

Microbiologic determinations were made at the pre-treatment visit. Microbiology was not reassessed at later visits. At the Day 11 and Day 30 visits, the following presumptive bacterial/clinical cure outcomes (i.e., clinical success) were obtained from the evaluable group:

Presumed Bacteriologic Eradication

	Day 11		Day 30	
	Azithromycin	Control	Azithromycin	Control
S. pneumoniae	25/29 (86%)	26/26 (100%)	22/28 (79%)	18/22 (82%)
H. influenzae	9/11 (82%)	9/9	8/10 (80%)	6/8
M. catarrhalis	7/7	5/5	5/5	2/3
S. pyogenes	2/2	5/5	2/2	4/4
Overall	43/49 (88%)	45/45 (100%)	37/45 (82%)	30/37 (81%)

In the safety analysis of the above study, the incidence of treatment-related adverse events, primarily gastrointestinal, in all patients treated was 4% with azithromycin and 31% with the control agent. The most common side effect was diarrhea/loose stools (2% azithromycin vs. 29% control).

Safety and efficacy using azithromycin 30 mg/kg given over 3 days

Protocol 4

In a double-blind, controlled, randomized clinical study of acute otitis media in pediatric patients from 6 months to 12 years of age, azithromycin (10 mg/kg per day for 3 days) was compared to amoxicillin/clavulanate potassium (7:1) in divided doses q12h for 10 days. Each patient received active drug and placebo matched for the comparator.

For the 366 patients who were evaluated for clinical efficacy at the Day 12 visit, the clinical success rate (i.e., cure plus improvement) was 83% for azithromycin and 88% for the control agent. For the 362 patients who were evaluated at the Day 24 to 28 visit, the clinical success rate was 74% for azithromycin and 69% for the control agent.

In the safety analysis of the above study, the incidence of treatment-related adverse events, primarily gastrointestinal, in all patients treated was 10.6% with azithromycin and 20% with the control agent. The most common side effects were diarrhea/loose stools (5.9% azithromycin vs. 14.6% control), vomiting (2.1% azithromycin vs. 1.1% control), and rash (0% azithromycin vs. 4.3% control).

Safety and efficacy using azithromycin 30 mg/kg given as a single dose

Protocol 5

A double blind, controlled, randomized trial was performed at nine clinical centers. Pediatric patients from 6 months to 12 years of age were randomized 1:1 to treatment with either azithromycin (given at 30 mg/kg as a single dose on Day 1) or amoxicillin/clavulanate potassium (7:1), divided q12h for 10 days. Each child received active drug, and placebo matched for the comparator.

Clinical response (Cure, Improvement, Failure) was evaluated at End of Therapy (Day 12 to 16) and Test of Cure (Day 28 to 32). Safety was evaluated throughout the trial for all treated subjects. For the 321 subjects who were evaluated at End of Treatment, the clinical success rate (cure plus improvement) was 87% for azithromycin, and 88% for the comparator. For the 305 subjects who were evaluated at Test of Cure, the clinical success rate was 75% for both azithromycin and the comparator.

In the safety analysis, the incidence of treatment-related adverse events, primarily gastrointestinal, was 16.8% with azithromycin, and 22.5% with the comparator. The most common side effects were diarrhea (6.4% with azithromycin vs. 12.7% with the comparator), vomiting (4% with each agent), rash (1.7% with azithromycin vs. 5.2% with the comparator) and nausea (1.7% with azithromycin vs. 1.2% with the comparator).

Protocol 6

In a non-comparative clinical and microbiological trial, 248 patients from 6 months to 12 years of age with documented acute otitis media were dosed with a single oral dose of azithromycin (30 mg/kg on Day 1).

For the 240 patients who were evaluable for clinical modified Intent-to-Treat (MITT) analysis, the clinical success rate (i.e., cure plus improvement) at Day 10 was 89% and for the 242 patients evaluable at Day 24 to 28, the clinical success rate (cure) was 85%.

Presumed Bacteriologic Eradication

	Day 10	Day 24 to 28
S. pneumoniae	70/76 (92%)	67/76 (88%)
H. influenzae	30/42 (71%)	28/44 (64%)
M. catarrhalis	10/10 (100%)	10/10 (100%)
Overall	110/128 (86%)	105/130 (81%)

In the safety analysis of this study, the incidence of treatment-related adverse events, primarily gastrointestinal, in all the subjects treated was 12.1%. The most common side effects were vomiting (5.6%), diarrhea (3.2%), and abdominal pain (1.6%).

Pharyngitis/Tonsillitis

In three double-blind controlled studies, conducted in the United States, azithromycin (12 mg/kg once a day for 5 days) was compared to penicillin V (250 mg three times a day for 10 days) in the treatment of pharyngitis due to documented Group A β-hemolytic streptococci (GABHS or *S. pyogenes*). Azithromycin was clinically and microbiologically statistically superior to penicillin at Day 14 and Day 30 with the following

clinical success (i.e., cure and improvement) and bacteriologic efficacy rates (for the combined evaluable patient with documented GABHS):

Three U.S. Streptococcal Pharyngitis Studies

Azithromycin vs. Penicillin V

EFFICACY RESULTS

	Day 14	Day 30
Bacteriologic Eradication:		
Azithromycin	323/340 (95%)	255/330 (77%)
Penicillin V	242/332 (73%)	206/325 (63%)
Clinical Success (Cure plus improvement):		
Azithromycin	336/343 (98%)	310/330 (94%)
Penicillin V	284/338 (84%)	241/325 (74%)

Approximately 1% of azithromycin-susceptible *S. pyogenes* isolates were resistant to azithromycin following therapy.

The incidence of treatment-related adverse events, primarily gastrointestinal, in all patients treated was 18% on azithromycin and 13% on penicillin. The most common side effects were diarrhea/loose stools (6% azithromycin vs. 2% penicillin), vomiting (6% azithromycin vs. 4% penicillin), and abdominal pain (3% azithromycin vs. 1% penicillin).

Adult Patients

Acute Bacterial Exacerbations of Chronic Obstructive Pulmonary Disease

In a randomized, double-blind controlled clinical trial of acute exacerbation of chronic bronchitis (AECB), azithromycin (500 mg once daily for 3 days) was compared with clarithromycin (500 mg twice daily for 10 days). The primary endpoint of this trial was the clinical cure rate at Day 21 to 24. For the 304 patients analyzed in the modified intent to treat analysis at the Day 21 to 24 visit, the clinical cure rate for 3 days of azithromycin was 85% (125/147) compared to 82% (129/157) for 10 days of clarithromycin.

The following outcomes were the clinical cure rates at the Day 21 to 24 visit for the bacteriologically evaluable patients by pathogen:

Pathogen	**Azithromycin**	**Clarithromycin**
	(3 Days)	**(10 Days)**
S. pneumoniae	29/32 (91%)	21/27 (78%)
H. influenzae	12/14 (86%)	14/16 (88%)
M. catarrhalis	11/12 (92%)	12/15 (80%)

In the safety analysis of this study, the incidence of treatment-related adverse events, primarily gastrointestinal, were comparable between treatment arms (25% with azithromycin and 29% with clarithromycin). The most common side effects were diarrhea, nausea, and abdominal pain with comparable incidence rates for each

symptom of 5 to 9% between the two treatment arms (see **ADVERSE REACTIONS**).

Acute Bacterial Sinusitis

In a randomized, double-blind, double-dummy controlled clinical trial of acute bacterial sinusitis, azithromycin (500 mg once daily for 3 days) was compared with amoxicillin/clavulanate (500/125 mg tid for 10 days). Clinical response assessments were made at Day 10 and Day 28. The primary endpoint of this trial was prospectively defined as the clinical cure rate at Day 28. For the 594 patients analyzed in the modified intent to treat analysis at the Day 10 visit, the clinical cure rate for 3 days of azithromycin was 88% (268/303) compared to 85% (248/291) for 10 days of amoxicillin/clavulanate. For the 586 patients analyzed in the modified intent to treat analysis at the Day 28 visit, the clinical cure rate for 3 days of azithromycin was 71.5% (213/298) compared to 71.5% (206/288), with a 97.5% confidence interval of -8.4 to 8.3, for 10 days of amoxicillin/clavulanate.

In the safety analysis of this study, the overall incidence of treatment-related adverse events, primarily gastrointestinal, was lower in the azithromycin treatment arm (31%) than in the amoxicillin/clavulanate arm (51%). The most common side effects were diarrhea (17% in the azithromycin arm vs. 32% in the amoxicillin/clavulanate arm), and nausea (7% in the azithromycin arm vs. 12% in the amoxicillin/clavulanate arm) (see **ADVERSE REACTIONS**).

In an open label, noncomparative study requiring baseline transantral sinus punctures the following outcomes were the clinical success rates at the Day 7 and Day 28 visits for the modified intent to treat patients administered 500 mg of azithromycin once daily for 3 days with the following pathogens:

Pathogen	**Azithromycin (500 mg per day for 3 Days)**	
	Day 7	***Day 28***
S. pneumoniae	23/26 (88%)	21/25 (84%)
H. influenzae	28/32 (87%)	24/32 (75%)
M. catarrhalis	14/15 (93%)	13/15 (87%)

The overall incidence of treatment-related adverse events in the noncomparative study was 21% in modified intent to treat patients treated with azithromycin at 500 mg once daily for 3 days with the most common side effects being diarrhea (9%), abdominal pain (4%) and nausea (3%) (see **ADVERSE REACTIONS**).

ANIMAL TOXICOLOGY

Phospholipidosis (intracellular phospholipid accumulation) has been observed in some tissues of mice, rats, and dogs given multiple doses of azithromycin. It has been demonstrated in numerous organ systems (e.g., eye, dorsal root ganglia, liver, gallbladder, kidney, spleen, and pancreas) in dogs treated with azithromycin at doses which, expressed on the basis of mg/m^2, are approximately equal to the recommended adult human dose, and in rats treated at doses approximately one-sixth of the recommended adult human dose. This effect has been shown to be reversible after

cessation of azithromycin treatment. Phospholipidosis has been observed to a similar extent in the tissues of neonatal rats and dogs given daily doses of azithromycin ranging from 10 days to 30 days. Based on the pharmacokinetic data, phospholipidosis has been seen in the rat (30 mg/kg dose) at observed C_{max} value of 1.3 mcg/mL (six times greater than the observed C_{max} of 0.216 mcg/mL at the pediatric dose of 10 mg/kg). Similarly, it has been shown in the dog (10 mg/kg dose) at observed C_{max} value of 1.5 mcg/mL (seven times greater than the observed same C_{max} and drug dose in the studied pediatric population). On a mg/m^2 basis, 30 mg/kg dose in the neonatal rat (135 mg/m^2) and 10 mg/kg dose in the neonatal dog (79 mg/m^2) are approximately 0.5 and 0.3 times, respectively, the recommended dose in the pediatric patients with an average body weight of 25 kg. Phospholipidosis, similar to that seen in the adult animals, is reversible after cessation of azithromycin treatment. The significance of these findings for animals and for humans is unknown.

REFERENCES

- Clinical and Laboratory Standards Institute (CLSI). Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard - Ninth Edition. CLSI document M07-A9. CLSI 950 West Valley Rd, Suite 250, Wayne, PA 19087, 2012.
- CLSI, Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Second Informational Supplement. CLSI document M100-S22**.** CLSI, Wayne, PA 19087, 2012.
- CLSI. Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard - Eleventh Edition. CLSI document M02-A11. CLSI, Wayne, PA 19087, 2012.

Manufactured In Croatia By:

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Zagreb, Croatia

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Sellersville, PA 18960

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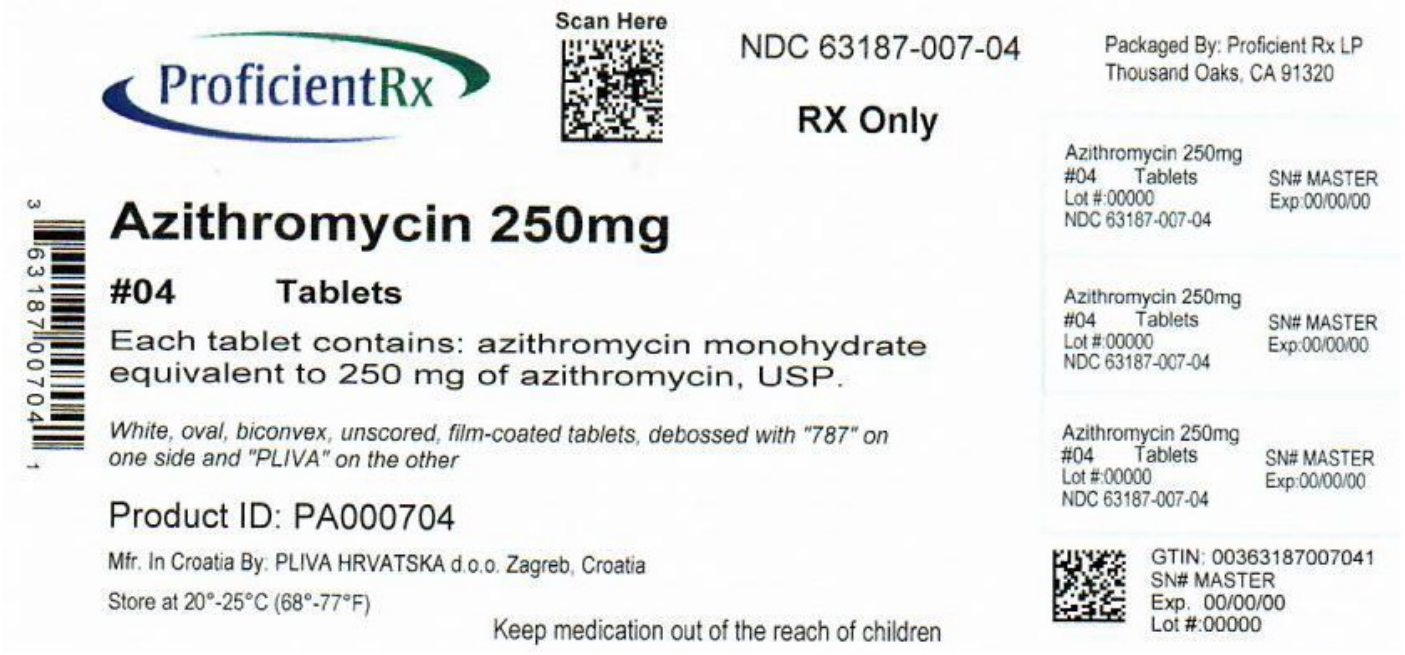
Proficient Rx LP

Thousand Oaks, CA 91320

PRINCIPAL DISPLAY PANEL, Part 1 of 2



PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

AZITHROMYCIN

azithromycin tablet, film coated

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:63187-007(NDC:50111-787)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
AZITHROMYCIN MONOHYDRATE (UNII: JTE4MNN1MD) (AZITHROMYCIN ANHYDROUS - UNII:J2KLZ20U1M)	AZITHROMYCIN ANHYDROUS	250 mg

Inactive Ingredients	
Ingredient Name	**Strength**
STARCH, CORN (UNII: O8232NY3SJ)	
ANHYDROUS DIBASIC CALCIUM PHOSPHATE (UNII: L11K75P92J)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
HYPROMELLOSE 2910 (15 MPA.S) (UNII: 36SFW2JZ0W)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POLYETHYLENE GLYCOL 4000 (UNII: 4R4HFI6D95)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics			
Color	WHITE	**Score**	no score
Shape	OVAL	**Size**	15mm
Flavor		**Imprint Code**	PLIVA;787
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:63187-007-04	4 in 1 BOTTLE; Type 0: Not a Combination Product	03/17/2022	
2	NDC:63187-007-06	1 in 1 BOX	10/01/2014	
2		6 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA065225	01/06/2006	

AZITHROMYCIN

azithromycin tablet, film coated

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:63187-189(NDC:50111-788)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AZITHROMYCIN MONOHYDRATE (UNII: JTE4MNN1MD) (AZITHROMYCIN ANHYDROUS - UNII:J2KLZ20U1M)	AZITHROMYCIN ANHYDROUS	500 mg

Inactive Ingredients

Ingredient Name	Strength
STARCH, CORN (UNII: O8232NY3SJ)	
ANHYDROUS DIBASIC CALCIUM PHOSPHATE (UNII: L11K75P92J)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
HYPROMELLOSE 2910 (15 MPA.S) (UNII: 36SFW2JZ0W)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POLYETHYLENE GLYCOL 4000 (UNII: 4R4HFI6D95)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics

Color	BLUE	**Score**	no score
Shape	OVAL (Capsule Shaped)	**Size**	19mm
Flavor		**Imprint Code**	PLIVA;788
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:63187-189-03	1 in 1 BOX	10/01/2014	
1		3 in 1 BLISTER PACK; Type 0: Not a Combination Product		
2	NDC:63187-189-04	4 in 1 BOTTLE; Type 0: Not a Combination Product	09/14/2022	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA065223	01/06/2006	

Labeler - Proficient Rx LP (079196022)

Establishment

Name	Address	ID/FEI	Business Operations
Proficient Rx LP		079196022	RELABEL(63187-007, 63187-189) , REPACK(63187-007, 63187-189)

Revised: 10/2022 Proficient Rx LP