Zithromax SD ®

Azithromycin

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U.S.A

Bahrain, Jordan, Kuwait, Lebanon, Oman, Qatar, UAE, Iran

US Prescribing Information and Medication

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Zithromax SD safely and effectively. See full prescribing information for Zithromax SD.

Zithromax SD (azithromycin extended-release) for oral suspension

----------RECENT MAJOR CHANGES----------
Warnings and Precautions, Hypersensitivity (5.1) 5/2016
Warnings and Precautions, Infantile Hypertrophic Pyloric Stenosis (5.3) 3/2017

----------INDICATIONS AND USAGE----------
Zithromax SD is a macrolide antimicrobial drug indicated for mild to moderate infections caused by designated, susceptible bacteria:
- Acute bacterial sinusitis in adults (1)
- Community-acquired pneumonia in adults (1)
- Limitation of Use
  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 (1.1).

To reduce the development of drug-resistant bacteria and maintain the effectiveness of **Zithromax SD** and other antibacterial drugs, **Zithromax SD** should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria

----------DOSAGE AND ADMINISTRATION----------
- Adults: 2 g as a single dose; consume contents of full bottle. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------
Bottle containing 2 g azithromycin for constitution with 60 mL of water (final concentration 27 mg/mL). (3)

----------CONTRAINDICATIONS----------
Hypersensitivity to azithromycin, erythromycin, or any macrolide or ketolide drug. (4.1)
History of cholestatic jaundice/hepatic dysfunction associated with prior use of azithromycin. (4.2)

----------WARNINGS AND PRECAUTIONS----------
- Allergic and Skin Reactions (including fatal): Discontinue Zithromax SD if reaction occurs. (5.1)
- Hepatotoxicity: severe, and sometimes fatal, hepatotoxicity has been reported. Discontinue immediately if signs and symptoms of hepatitis occur. (5.2)
- Prolongation of the QT interval and cases of torsades de pointes have been reported. This risk which can be fatal should be considered in patients with certain cardiovascular disorders including known QT prolongation or history of torsades de pointes, those with proarrhythmic conditions, and with other drugs that prolong the QT interval. (5.4)
- *Clostridium difficile*-Associated Diarrhea: Evaluate patients if diarrhea occurs. (5.5)
- Zithromax SD may exacerbate muscle weakness in persons with myasthenia gravis. (5.6)
- Gastrointestinal Disturbances: higher incidence in patients with GFR<10 mL/min. (5.7)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence ≥1%) are diarrhea/loose stools, nausea, abdominal pain, headache, and vomiting. (6.1, 6.2)

----------DRUG INTERACTIONS----------
- Nelfinavir: Close monitoring for known adverse reactions of azithromycin, such as liver enzyme abnormalities and hearing impairment, is warranted. (7.1)
- Warfarin: Use with azithromycin may increase coagulation times; monitor prothrombin time. (7.2)

----------USE IN SPECIFIC POPULATIONS----------
- Geriatric use: Elderly patients may be more susceptible to development of torsades de pointes arrhythmias. (8.5)

See 17 for PATIENT COUNSELING INFORMATION and patient labeling.

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Acute Bacterial Sinusitis in Adults and Community-Acquired Pneumonia

Zithromax SD (azithromycin) is a macrolide antibacterial drug indicated for the treatment of Patients with mild to moderate infections caused by susceptible strains of the designated microorganisms in the specific conditions listed below. *[See Clinical Studies (14)]*

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

Community-acquired pneumonia in adults due to *Chlamydophila pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae* or *Streptococcus pneumoniae,* in patients appropriate for oral therapy. *[See Use in Specific Populations (8.4)]*

1.2 Limitations of Use

Zithromax SD is not recommended for use 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 nosocomial 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).

1.3 Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Zithromax SD (azithromycin) and other antibacterial drugs, Zithromax SD (azithromycin) should be used only to treat 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.

2 DOSAGE AND ADMINISTRATION

2.1 Adults

Zithromax SD should be taken as a single 2 g dose. Zithromax SD provides a full course of antibacterial therapy in a single oral dose. It is recommended that Zithromax SD be taken on an empty stomach (at least 1 hr before or 2 hr following a meal).

2.2 Additional Treatment after Vomiting with Zithromax SD

In the event that a patient vomits within 5 minutes of administration, the health care provider should consider additional antibiotic treatment since there would be minimal absorption of azithromycin. Since insufficient data exist on absorption of azithromycin if a patient vomits between 5 and 60 minutes following administration, alternative therapy should be considered. Neither a second dose

of Zithromax SD nor alternative treatment is warranted if vomiting occurs ≥60 minutes following administration, in patients with normal gastric emptying. In patients with delayed gastric emptying, alternative therapy should be considered.

2.3 Instructions for the Pharmacist

Constitute with 60 mL of water and replace cap. Shake bottle well before dispensing. Do not refrigerate. Constituted suspension should be consumed within 12 hr.

3 DOSAGE FORMS AND STRENGTHS

Each bottle of Zithromax SD contains azithromycin dihydrate equivalent to 2 g of azithromycin. After constitution with 60 mL of water, each mL of suspension contains 27 mg of azithromycin. The suspension is a white or off-white color and has a cherry/banana flavor.

4 CONTRAINDICATIONS

4.1 Hypersensitivity Reactions

Zithromax SD is contraindicated in patients with known hypersensitivity to azithromycin, erythromycin or any macrolide or ketolide drug.

4.2 Cholestatic Jaundice/Hepatic Dysfunction

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

5 WARNINGS AND PRECAUTIONS

5.1 Allergic and Skin Reactions

Serious allergic reactions, including angioedema, anaphylaxis, Acute Generalized Exanthematous Pustulosis (AGEP), Stevens Johnson syndrome, and toxic epidermal necrolysis have been reported in patients on azithromycin therapy using other formulations. Fatalities have been reported. Cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) have also been reported. 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 exposure to antigen has not been determined.

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

5.2 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.

5.3 QT Prolongation

Prolonged cardiac repolarization and QT interval, imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen in treatment with macrolides, including azithromycin. Cases of torsades 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 torsades 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.

5.4 *Clostridium difficile*-Associated Diarrhea (CDAD)

Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Zithromax SD, 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.

5.5 Exacerbation of Myasthenia Gravis

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

5.6 Gastrointestinal Disturbances

A higher incidence of gastrointestinal adverse events (8 of 19 subjects) was observed when Zithromax SD was administered to a limited number of subjects with GFR<10 mL/min. *[See Use in Specific Populations (8.5)]*

5.7 Development of Drug Resistant Bacteria

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

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adults:

The data described below reflect exposure to Zithromax SD in 728 adult patients. All patients received a single 2 g oral dose of Zithromax SD. The population studied had community-acquired pneumonia and acute bacterial sinusitis.

In controlled clinical trials with Zithromax SD, the majority of the reported treatment-related adverse reactions were gastrointestinal in nature and mild to moderate in severity.

Overall, the most common treatment-related adverse reactions in adult patients receiving a single 2 g dose of Zithromax SD were diarrhea/loose stools (12%), nausea (4%), abdominal pain (3%), headache (1%), and vomiting (1%). The incidence of treatment-related gastrointestinal adverse reactions was 17% for Zithromax SD and 10% for pooled comparators.

Treatment-related adverse reactions following Zithromax SD treatment that occurred with a frequency of <1% included the following:

Cardiovascular: Palpitations, chest pain
Gastrointestinal: Constipation, dyspepsia, flatulence, gastritis, oral moniliasis
Genitourinary: Vaginitis
Nervous system: Dizziness, vertigo
General: Asthenia
Allergic: Rash, pruritus, urticaria
Special senses: Taste perversion

6.2 Postmarketing Experience with Other Azithromycin Products

Because these reactions are reported voluntarily from a population of uncertain size, reliably estimating their frequency or establishing a causal relationship to drug exposure is not always possible.

Adverse events reported with azithromycin immediate release formulations during the postmarketing period for which a causal relationship may not be established include:

Allergic: Arthralgia, edema, urticaria and angioedema
Cardiovascular: Palpitations and arrhythmias including ventricular tachycardia and hypotension
There have been reports of QT prolongation and *torsades de pointes*.
Gastrointestinal: Anorexia, constipation, dyspepsia, flatulence, vomiting/diarrhea, pseudomembranous colitis, pancreatitis, oral candidiasis, pyloric stenosis, and rare reports of tongue discoloration
General: Asthenia, paresthesia, fatigue, malaise and anaphylaxis
Genitourinary: Interstitial nephritis, acute renal failure and vaginitis
Hematopoietic: Thrombocytopenia, mild neutropenia

Liver/biliary: Adverse reactions related to hepatic dysfunction have been reported in postmarketing experience with azithromycin. *[See Warnings and Precautions (5.2)]*
Nervous system: Convulsions, dizziness/vertigo, headache, somnolence, hyperactivity, nervousness, agitation and syncope
Psychiatric: Aggressive reaction and anxiety
Skin/appendages: Pruritus, rash, photosensitivity, serious skin reactions including erythema multiforme, AGEP, Stevens-Johnson syndrome, toxic epidermal necrolysis, and DRESS.
Special senses: Hearing disturbances including hearing loss, deafness and/or tinnitus and reports of taste/smell perversion and/or loss

6.3 Laboratory Abnormalities
In subjects with normal baseline values, the following clinically significant laboratory abnormalities (irrespective of drug relationship) were reported in Zithromax SD clinical trials in adults:

Adults:
Laboratory abnormalities with an incidence of greater than or equal to 1%: reduced lymphocytes and increased eosinophils; reduced bicarbonate. Laboratory abnormalities with an incidence of less than 1%: leukopenia, neutropenia, elevated bilirubin, AST, ALT, BUN, creatinine, alterations in potassium. Where follow-up was provided, changes in laboratory tests appeared to be reversible.

7 DRUG INTERACTIONS

7.1 Nelfinavir
Co-administration 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 adverse reactions of azithromycin, such as liver enzyme abnormalities and hearing impairment, is warranted. *[see Adverse Reactions (6)]*

7.2 Warfarin
Spontaneous post-marketing reports suggest that concomitant administration of azithromycin may potentiate the effects of oral anticoagulants such as warfarin, although the prothrombin time was not affected in the dedicated drug interaction study with azithromycin and warfarin. Prothrombin times should be carefully monitored while patients are receiving azithromycin and oral anticoagulants concomitantly.

7.3 Potential Drug-Drug Interactions with Macrolides
Interactions with digoxin or phenytoin have not been reported in clinical trials with azithromycin; however, no specific drug interaction studies have been performed to evaluate potential drug-drug interactions. However, drug interactions have been observed with other macrolide products. Until further data are developed regarding drug interactions when digoxin or phenytoin are used concomitantly with azithromycin careful monitoring of patients is advised.

8 USE IN SPECIFIC POPULATIONS

8.1 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 daily

doses in rats and mice, based on body surface area, are estimated to be approximately equivalent to one or one-half of, respectively, the single adult oral dose of 2 g. 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.

8.3 Nursing Mothers

Azithromycin has been reported to be excreted in human breast milk in small amounts. Caution should be exercised when azithromycin is administered to a nursing woman.

8.4 Geriatric Use

Data collected from the azithromycin capsule and tablet formulations indicate that a dosage adjustment does not appear to be necessary for older patients with normal renal function (for their age) and hepatic function receiving treatment with Zithromax SD.

In clinical trials of Zithromax SD, 17% of subjects were at least 65 years of age (214/1292) and 5% of subjects (59/1292) were at least 75 years of age. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Elderly patients may be more susceptible to development of torsades de pointes arrhythmia than younger patients. *[See Warnings and Precautions (5.3)]*

8.5 Renal Impairment

No dosage adjustment is recommended for patients GFR >10 mL/min. Caution should be exercised when Zithromax SD is administered to patients with GFR <10 mL/min, due to a higher incidence of gastrointestinal adverse events (8 of 19 subjects) observed in a limited number of subjects with GFR <10 mL/min. *[See Clinical Pharmacology (12)]*

8.6 Gender

The impact of gender on the pharmacokinetics of azithromycin has not been evaluated for Zithromax SD. However, previous studies have demonstrated no significant differences in the disposition of azithromycin between male and female subjects. No dosage adjustment of Zithromax SD is recommended based on gender.

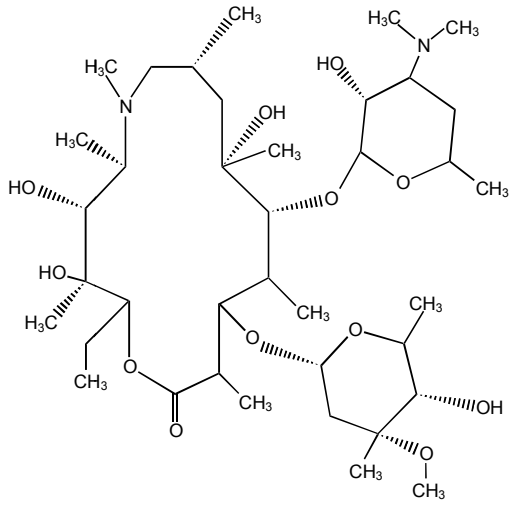
10 OVERDOSAGE

Adverse reactions experienced at higher than recommended doses were similar to those seen at normal doses. In the event of overdosage, general symptomatic and supportive measures are indicated as required.

11 DESCRIPTION

Zithromax SD (azithromycin extended-release) for oral suspension contains the active ingredient azithromycin (as azithromycin dihydrate), an azalide, a subclass of macrolide antibacterial drug. Azithromycin 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 is

derived from erythromycin; however, it differs chemically from erythromycin in that a methyl-substituted nitrogen atom is incorporated into the lactone ring. Its molecular formula is $C_{38}H_{72}N_2O_{12}$, and its molecular weight is 749.0. Azithromycin has the following structural formula:



Azithromycin, as the dihydrate, is a white crystalline powder with a molecular formula of $C_{38}H_{72}N_2O_{12}\bullet 2H_2O$ and a molecular weight of 785.0.

Zithromax SD is a single-dose, extended-release formulation of microspheres for oral suspension containing azithromycin (as azithromycin dihydrate) and the following excipients: glyceryl behenate, poloxamer 407, sucrose, sodium phosphate tribasic anhydrous, magnesium hydroxide, hydroxypropyl cellulose, xanthan gum, colloidal silicon dioxide, titanium dioxide, artificial cherry flavor, and artificial banana flavor.

Note: Each bottle of Zithromax SD 2 g for oral suspension contains approximately 148 mg of sodium and 19 g of sucrose. Constituted Zithromax SD oral suspension contains approximately 2 mg/mL of sodium and 0.26 g/mL of sucrose.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Azithromycin is a macrolide antibacterial drug. *[See Clinical Pharmacology (12.4)]*

12.2 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). Co-administration 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 co-administration of 500 mg, 1000 mg and 1500 mg azithromycin, respectively.

12.3 Pharmacokinetics

Zithromax SD is an extended-release microsphere formulation. Based on data obtained from studies evaluating the pharmacokinetics of azithromycin in healthy adult subjects a higher peak serum concentration (C_{max}) and greater systemic exposure (AUC_{0-24}) of azithromycin are achieved on the day of dosing following a single 2 g dose of Zithromax SD versus 1.5 g of azithromycin tablets administered over 3 days (500 mg/day) or 5 days (500 mg on day 1, 250 mg/day on days 2-5) [Table 2]. Consequently, due to these different pharmacokinetic profiles, Zithromax SD is not interchangeable with azithromycin tablet 3-day and 5-day dosing regimens.

Table 2. Mean (SD) Pharmacokinetic Parameters for Azithromycin on Day 1 Following the Administration of a Single Dose of 2 g Zithromax SD or 1.5 g of Azithromycin Tablets Given over 3 Days (500 mg/day) or 5 Days (500 mg on Day 1 and 250 mg on Days 2-5) to Healthy Adult Subjects

Pharmacokinetic Parameter*	Azithromycin Regimen		
	Zithromax SD [N=41]†	3-day ‡ [N=12]	5-day ‡ [N=12]
C_{max} (mcg/mL)	0.821 (0.281)	0.441 (0.223)	0.434 (0.202)
T_{max} § (hr)	5.0 (2.0-8.0)	2.5 (1.0-4.0)	2.5 (1.0-6.0)
AUC_{0-24} (mcg·hr/mL)	8.62 (2.34)	2.58 (0.84)	2.60 (0.71)
$AUC_{0-\infty}$ (mcg·hr/mL)	20.0 (6.66)	17.4 (6.2)	14.9 (3.1)
$t_{1/2}$ (hr)	58.8 (6.91)	71.8 (14.7)	68.9 (13.8)

* Zithromax SD, 3-day and 5-day regimen parameters obtained from separate pharmacokinetic studies
† N = 21 for $AUC_{0-\infty}$ and $t_{1/2}$
‡ C_{max}, T_{max} and AUC_{0-24} values for Day 1 only
§ Median (range)
¶ Total AUC for the 1-day, 3-day and 5-day regimens
SD = standard deviation
C_{max} = maximum serum concentration
T_{max} = time to C_{max}
AUC = area under concentration vs. time curve
$t_{1/2}$ = terminal serum half-life

Absorption
The bioavailability of Zithromax SD relative to azithromycin immediate release (IR) (powder for oral suspension) was 83%. On average, peak serum concentrations were achieved approximately 2.5 hr later following Zithromax SD administration and were lower by 57%, compared to 2 g azithromycin IR. Thus, single 2 g doses of Zithromax SD and azithromycin IR are not bioequivalent and are not interchangeable.

Effect of food on absorption: A high-fat meal increased the rate and extent of absorption of a 2 g dose of Zithromax SD (115% increase in C_{max}, and 23% increase in AUC_{0-72}) compared to the fasted state. A standard meal also increased the rate of absorption (119% increase in C_{max}) and with less effect on the

extent of absorption (12% increase in AUC_{0-72}) compared to administration of a 2 g Zithromax SD dose in the fasted state.

Effect of antacids: Following the administration of Zithromax SD with an aluminum and magnesium hydroxide antacid, the rate and extent of azithromycin absorption were not altered.

Distribution
The serum protein binding of azithromycin is concentration dependent, 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.

Azithromycin concentrates in fibroblasts, epithelial cells, macrophages, and circulating neutrophils and monocytes. Higher azithromycin concentrations in tissues than in plasma or serum have been observed. White blood cell and lung exposure data in humans following a single 2 g dose of Zithromax SD in adults are shown in Table 3. Following a 2 g single dose of Zithromax SD, azithromycin achieved higher exposure (AUC_{0-120}) in mononuclear leukocytes (MNL) and polymorphonuclear leukocytes (PMNL) than in serum. The azithromycin exposure (AUC_{0-72}) in lung tissue and alveolar cells (AC) was approximately 100 times that in serum; and the exposure in epithelial lining fluid (ELF) was also higher (approximately 2-3 times) than in serum. The clinical significance of this distribution data is unknown.

Table 3. Azithromycin Exposure Data in White Blood Cells and Lung Following a 2 g Single Dose of Zithromax SD in Adults

A single 2 g dose of Zithromax SD				
WBC	C_{max} (mcg/mL)	AUC_{0-24} (mcg·hr/mL)	AUC_{0-120} (mcg·hr/mL)	$C_{t=120}$ † (mcg/mL)
MNL‡	116 (40.2)	1790 (540)	4710 (1100)	16.2 (5.51)
PMNL‡	146 (66.0)	2080 (650)	10000 (2690)	81.7 (23.3)
LUNG	C_{max} (mcg/mL)	AUC_{0-24} (mcg·hr/mL)	AUC_{0-72} (mcg·hr/mL)	
ALVEOLAR CELL¶	669	7028	20403	-
ELF¶	3.2	17.6	131	-
	C_{max} (mcg/g)	AUC_{0-24} (mcg·hr/g)	AUC_{0-72} (mcg·hr/g)	
LUNG TISSUE¶	37.9	505	1693	-

Abbreviation: WBC: white blood cells; MNL: mononuclear leukocytes; PMNL: polymorphonuclear leukocytes; ELF: Epithelial lining fluid
† Azithromycin concentration at 120 hr after the start of dosing
‡ Data are presented as mean (standard deviation)
¶ C_{max} and AUC were calculated based on composite profile (n = 4 subjects/time point/formulation).

Following a regimen of 500 mg of azithromycin tablets 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.

Excretion
Serum azithromycin concentrations following a single 2 g dose of Zithromax SD declined in a polyphasic pattern with a terminal elimination half-life of 59 hr. The prolonged terminal half-life is thought to be due to a large apparent volume of distribution.

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.

Specific 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 1.0 g dose of azithromycin (4 × 250 mg capsules), the mean C_{max} and AUC_{0-120} were 5.1% and 4.2% higher, respectively in subjects with 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} were 61% and 35% higher, respectively in subjects with GFR <10 mL/min compared to subjects with normal renal function. *[See Use in Specific Populations Renal Impairment (8.5)]*

Hepatic Insufficiency
The pharmacokinetics of azithromycin in subjects with hepatic impairment has not been established.

Table 4. Mean (SD) Pharmacokinetic Parameters for Azithromycin Following Administration of a Single Dose of Zithromax SD (60 mg/kg, maximum dose of 2 g) to Pediatric Subjects Aged 3 Months to 16 Years

Treatment Group	Pharmacokinetic Parameters			
	C_{max} (mcg/mL)	**T_{max}* (hr)**	**$AUC_{(0-24)}$ (mcg·hr/mL)**	**$AUC_{(0-\infty)}$ (mcg·hr/mL)**
Group 1 (N = 6) [3 to 18 months]	0.74 (0.20)	3 (3-3)	6.29 (1.17)	14.1 (2.16) (n = 3)
Group 2† (N = 6) [>18 to 36 months]	1.88† (0.50)	3 (3-3)	19.7† (5.35)	37.3 (12.9) (n = 5)

Group 3 (N = 6) [>36 to 48 months]	1.23 (0.42)	3 (3-6)	12.9 (3.79)	22.4 (5.96)
Group 4 (N = 6) [>48 months to 8 years]	1.13 (0.34)	3 (3-6)	13.0 (4.21)	22.2 (6.89)
Group 5 (N = 6) [>8 to 12 years]	1.65 (0.38)	3 (3-6)	16.0 (4.99)	30.1 (10.7)
Group 6 (N = 6) [>12 to 16 years]	0.98 (0.35)	3 (3-6)	11.0 (4.78)	21.3 (9.37)
Pooled 1-6 (N = 36) [On an empty stomach]	1.27 (0.53)	3 (3-6)	13.1 (5.78)	25.2 (10.7) (n = 32)
Group 7‡ (N = 7) [Fed; 18 months to 8 years]	1.41 (0.62)	3 (1.5-3.1)	7.43 (3.00)	18.9 (3.57) (n = 3)

Empty stomach = dosed with Zithromax SD at least 1 hr before or 2 hr after a meal (Groups I-VI)
Fed = dosed with Zithromax SD within 5 minutes of consuming an age-appropriate high-fat breakfast (Group VII)
* Median (range) presented only for T_{max}
† High mean values were driven by 2 subjects with high exposure
‡ One subject vomited immediately after dosing and discontinued from the study

Gender

The impact of gender on the pharmacokinetics of azithromycin has not been evaluated for Zithromax SD. However, previous studies have demonstrated no significant differences in the disposition of azithromycin between male and female subjects.

Pharmacokinetic Interaction Studies

A drug interaction study was performed with Zithromax SD and antacids. All other drug interaction studies were performed with azithromycin immediate release (IR) formulations (capsules and tablets, doses ranging from 500 to 1200 mg) and other drugs likely to be co-administered. The effects of co-administration of azithromycin on the pharmacokinetics of other drugs are shown in Table 5 and the effects of other drugs on the pharmacokinetics of azithromycin are shown in Table 6.

When used at therapeutic doses, azithromycin IR had a minimal effect on the pharmacokinetics of atorvastatin, carbamazepine, cetirizine, didanosine, efavirenz, fluconazole, indinavir, midazolam, nelfinavir, sildenafil, theophylline (intravenous and oral), triazolam, trimethoprim/sulfamethoxazole or zidovudine (Table 5). Although the drug interaction studies were not conducted with Zithromax SD, similar modest effect as observed with IR formulation are expected since the total exposure to azithromycin is comparable for Zithromax SD and other azithromycin IR regimens. Therefore, no dosage adjustment of drugs listed in Table 5 is recommended when co-administered with Zithromax SD.

Nelfinavir significantly increased the C_{max} and AUC of azithromycin following co-administration with azithromycin IR 1200 mg (Table 6). However, no dose adjustment of azithromycin is recommended when Zithromax SD is co-administered with nelfinavir.

Pharmacokinetic and/or pharmacodynamic 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, pharmacokinetic and/or pharmacodynamic interactions with these drugs have been observed with other macrolide products. Until further data are developed, careful monitoring of patients is advised when azithromycin and these drugs are used concomitantly: digoxin, ergotamine or dihydroergotamine, cyclosporine, hexobarbital and phenytoin.

Table 5. Drug Interactions: Pharmacokinetic Parameters of Co-administered Drugs in the Presence of Azithromycin

Co-administered Drug	Dose of Co-administered Drug	Dose of Azithromycin*	n	Ratio (with/without Azithromycin) of Co-administered Drug Pharmacokinetic Parameters (90% CI); No Effect = 1.00	
				Mean C_{max}	Mean AUC
Atorvastatin	10 mg/day for 8 days	500 mg/day orally on days 6-8	12	0.83 (0.63 to 1.08)	1.01 (0.81 to 1.25)
Carbamazepine	200 mg/day for 2 days, then 200 mg twice a day for 18 days	500 mg/day orally for days 16-18	7	0.97 (0.88 to 1.06)	0.96 (0.88 to 1.06)
Cetirizine	20 mg/day for 11 days	500 mg orally on day 7, then 250 mg/day on days 8-11	14	1.03 (0.93 to 1.14)	1.02 (0.92 to 1.13)
Didanosine	200 mg orally twice a day for 21 days	1,200 mg/day orally on days 8-21	6	1.44 (0.85 to 2.43)	1.14 (0.83 to 1.57)
Efavirenz	400 mg/day for 7 days	600 mg orally on day 7	14	1.04†	0.95†
Fluconazole	200 mg orally single dose	1,200 mg orally single dose	18	1.04 (0.98 to 1.11)	1.01 (0.97 to 1.05)
Indinavir	800 mg three times a day for 5 days	1,200 mg orally on day 5	18	0.96 (0.86 to 1.08)	0.90 (0.81 to 1.00)
Midazolam	15 mg orally on day 3	500 mg/day orally for 3 days	12	1.27 (0.89 to 1.81)	1.26 (1.01 to 1.56)
Nelfinavir	750 mg three times a day for 11 days	1,200 mg orally on day 9	14	0.90 (0.81 to 1.01)	0.85 (0.78 to 0.93)
Sildenafil	100 mg on days 1 and 4	500 mg/day orally for 3 days	12	1.16 (0.86 to 1.57)	0.92 (0.75 to 1.12)
Theophylline	4 mg/kg IV on days 1, 11, 25	500 mg orally on day 7, then 250 mg/day on days 8-11	10	1.19 (1.02 to 1.40)	1.02 (0.86 to 1.22)
Theophylline	300 mg orally twice a day for 15 days	500 mg orally on day 6, then 250 mg/day on days 7-10	8	1.09 (0.92 to 1.29)	1.08 (0.89 to 1.31)
Triazolam	0.125 mg on day 2	500 mg orally on day 1, then 250 mg/day on day 2	12	1.06†	1.02†
Trimethoprim/ Sulfamethoxazole	160 mg/800 mg/day orally for 7 days	1,200 mg orally 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 orally for 21 days	600 mg/day oraly for 14 days	5	1.12 (0.42 to 3.02)	0.94 (0.52 to 1.70)
Zidovudine	500 mg/day orally for 21 days	1,200 mg/day orally for 14 days	4	1.31 (0.43 to 3.97)	1.30 (0.69 to 2.43)

* Refers to azithromycin capsules and tablets unless specified
† 90% confidence interval not reported

Table 6. Drug Interactions: Pharmacokinetic Parameters of Azithromycin in the Presence of Co-administered Drugs

Co-administered Drug	Dose of Co-administered Drug	Dose of Azithromycin*	n	Ratio (with/without co-administered drug) of Azithromycin Pharmacokinetic Parameters (90% CI); No Effect = 1.00	
				Mean C_{max}	Mean AUC
Efavirenz	400 mg/day for 7 days	600 mg orally on day 7	14	1.22 (1.04 to 1.42)	0.92†
Fluconazole	200 mg orally single dose	1,200 mg orally single dose	18	0.82 (0.66 to 1.02)	1.07 (0.94 to 1.22)
Nelfinavir	750 mg three times a day 11 days	1,200 mg orally on day 9	14	2.36 (1.77 to 3.15)	2.12 (1.80 to 2.50)
Aluminum and Magnesium hydroxide	20 mL regular strength, single dose	2 g Zithromax SD, single dose	39	0.99 (0.93 to 1.06)	0.99 (0.92 to 1.08)

* Refers to azithromycin capsules and tablets unless specified
† 90% confidence interval not reported

12.4 Microbiology

Mechanism of Action
Azithromycin acts by binding to the 23S rRNA of the 50S ribosomal subunit of susceptible microorganisms inhibiting bacterial protein synthesis and impeding the assembly of the 50S ribosomal subunit.

Resistance
Azithromycin demonstrates cross resistance with erythromycin. The most frequently encountered mechanism of resistance to azithromycin is modification of the 23S rRNA target, most often by methylation. Ribosomal modifications can determine cross resistance to other macrolides, lincosamides and streptogramin B (MLS_B phenotype).

Azithromycin has been shown to be active against the following microorganisms, both *in vitro* and in clinical infections. *[See Indications and Usage (1)]*.

Gram-Positive Bacteria
Streptococcus pneumoniae

Gram-Negative Bacteria
Haemophilus influenzae
Moraxella catarrhalis

"Other" Bacteria
Chlamydophila pneumoniae
Mycoplasma pneumoniae

Susceptibility Testing Methods
When available, the clinical microbiology laboratory should provide cumulative reports of *in vitro* susceptibility test results for antimicrobial products used in local hospitals and practice areas to the

physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibacterial drug for treatment.

Dilution Techniques

Quantitative methods are used to determine antimicrobial MICs. These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized test method [1,2,3,4] (broth and/or agar). The MIC values should be interpreted according to criteria provided in Table 7.

Diffusion Techniques

Quantitative methods that require measurement of zone diameters can provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size should be determined using a standardized method [2,3,4]. This procedure uses paper disk impregnated with 15 mcg azithromycin to test the susceptibility of bacteria to azithromycin. The disk diffusion breakpoints are provided in Table 7.

Table 7: Susceptibility Interpretive Criteria for Azithromycin

Pathogen	Minimum Inhibitory Concentrations (mcg/mL)			Disk Diffusion (zone diameter in mm)		
	S	I	R	S	I	R
*Haemophilus influenzae**	≤4	-	-	≥12	-	-
*Moraxella catarrhalis**	≤0.25	-	-	≥26	-	-
Streptococcus pneumoniae	≤0.5	1	≥2	≥18	14-17	≤13

* Insufficient information is available to determine Intermediate or Resistant interpretive criteria

A report of *Susceptible (S)* indicates that the antimicrobial drug is likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration usually achievable at the site of infection. A report of *Intermediate (I)* 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 a high dosage of the drug can be used. This category also provides a buffer zone that prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of *Resistant (R)* indicates that the antimicrobial drug is not likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentrations usually achievable at the infection site; 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 individuals performing the test [1,2,3,4]. Standard azithromycin powder should provide the following range of MIC values provided in Table 8. For the diffusion technique using the 15-mcg azithromycin disk the criteria provided in Table 8 should be achieved.

Table 8: Acceptable Quality Control Ranges for Susceptibility Testing

Quality Control Organism	Minimum Inhibitory Concentrations (mcg/mL)	Disk Diffusion (zone diameters in mm)
Haemophilus Influenzae		

ATCC* 49247	1-4	13-21
Staphylococcus aureus ATCC 25923	Not Applicable	21-26
Staphylococcus aureus ATCC 29213	0.5-2	Not Applicable
Streptococcus pneumoniae ATCC 49619	0.06-0.25	19-25
Neisseria gonorrhoeae ATCC 49226	0.25-1	Not Applicable

*ATCC = American Type Culture Collection

13 NONCLINICAL TOXICOLOGY

13. 1 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 in rats given daily doses up to 10 mg/kg (approximately 0.05 times the single 2 g oral adult human dose based on body surface area).

13. 2 Animal Toxicology and/or Pharmacology

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/or pancreas) in dogs treated with azithromycin at doses which, expressed on the basis of mg/m^2, are approximately one-sixth the recommended adult dose, and in rats treated at doses approximately one-fourth the recommended adult dose. This effect has been shown to be reversible after cessation of azithromycin treatment. Based on the pharmacokinetic data, phospholipidosis has been seen in the rat (50 mg/kg/day dose) at the observed maximal plasma concentration of 1.3 mcg/mL (1.6 times the observed C_{max} of 0.821 mcg/mL at the adult dose of 2 g.). Similarly, it has been shown in the dog (10 mg/kg/day dose) at the observed maximal serum concentration of 1 mcg/mL (1.2 times the observed C_{max} of 0.821 mcg/mL at the adult dose of 2 g).

Phospholipidosis was also observed in neonatal rats dosed for 18 days at 30 mg/kg/day, which is less than the pediatric dose of 60 mg/kgbased on the surface area. It was not observed in neonatal rats treated for 10 days at 40 mg/kg/day with mean maximal serum concentrations of 1.86 mcg/mL, approximately 1.5 times the C_{max} of 1.27 mcg/mL at the pediatric dose. Phospholipidosis has been observed in neonatal dogs (10 mg/kg/day) at maximum mean whole blood concentrations of 3.54 mcg/mL, approximately 3 times the pediatric dose C_{max}.

The significance of the finding for animals and for humans is unknown.

14 CLINICAL STUDIES

14.1 Acute Bacterial Maxillary Sinusitis

Adult subjects with a diagnosis of acute bacterial maxillary sinusitis were evaluated in a randomized, double-blind, multicenter study; a maxillary sinus tap was performed on all subjects at baseline. Clinical evaluations were conducted for all subjects at the TOC visit, 7 to 14 days post-treatment. Two

hundred seventy (270) subjects were treated with a single 2 g oral dose of Zithromax SD and 268 subjects were treated with levofloxacin, 500 mg orally once daily for 10 days. A subject was considered a cure if signs and symptoms related to the acute infection had resolved, or if clinical improvement was such that no additional antibiotics were deemed necessary. The clinical response for the primary population, Clinical Per Protocol Subjects, is presented below.

Table 9: Clinical Response in Patients with Acute Bacterial Maxillary Sinusitis

	ZITHROMAX SD	**LEVOFLOXACIN**
RESPONSE AT TOC	N = 255	N = 254
CURE	241 (94.5%)	236 (92.9%)
FAILURE	14 (5.5%)	18 (7.1%)

Clinical response by pathogen in the Bacteriologic Per Protocol population is presented below.

Table 10: Clinical Response by Pathogen in Patients with Acute Bacterial Maxillary Sinusitis

	Zithromax SD		**Levofloxacin**	
Pathogen	N	Cure	N	Cure
S. pneumoniae	37	36 (97.3%)	39	36 (92.3%)
H. influenzae	27	26 (96.3%)	30	30 (100.0%)
M. catarrhalis	8	8 (100.0%)	11	10 (90.9%)

14.2 Community-Acquired Pneumonia

Adult subjects with a diagnosis of mild-to-moderate community-acquired pneumonia were evaluated in two, randomized, double-blind, multicenter studies. In both studies, clinical and microbiologic evaluations were conducted for all subjects at the Test of Cure (TOC) visit, 7 to 14 days post-treatment. In Trial 1, 247 subjects were treated with a single 2 g oral dose of Zithromax SD and 252 subjects were treated with clarithromycin extended-release, 1 g orally once daily for 7 days. In Trial 2, 211 subjects were treated with a single 2.0 g oral dose of Zithromax SD and 212 subjects were treated with levofloxacin, 500 mg orally once daily for 7 days. A patient was considered a cure if signs and symptoms related to the acute infection had resolved, or if clinical improvement was such that no additional antibiotics were deemed necessary; in addition, the chest x-ray performed at the TOC visit was to be either improved or stable. The clinical response at TOC for the primary population, Clinical Per Protocol Subjects, is presented in the table below.

Table 11: Clinical Response at Test of Cure (TOC) in Patients with Community-Acquired Pneumonia

	ZITHROMAX SD	**Comparator**
ZITHROMAX SD **vs. Clarithromycin extended-release**	N=202	N=209
Cure	187 (92.6%)	198 (94.7%)
Failure	15 (7.4%)	11 (5.3%)
ZITHROMAX SD **vs. Levofloxacin**	N=174	N=189
Cure	156 (89.7%)	177 (93.7%)
Failure	18 (10.3%)	12 (6.3%)

Clinical response by pathogen in the Bacteriologic Per Protocol population, across both studies, is presented below:

Table 12: Clinical Response by Pathogen in Patients with Community-Acquired Pneumonia

Pathogen	**Zithromax SD**		**Comparators**	
	N	Cure	N	Cure
S. pneumoniae	33	28 (84.8%)	39	35 (89.7%)
H. influenzae	30	28 (93.3%)	34	31 (91.2%)
C. pneumoniae	40	37 (92.5%)	53	50 (94.3%)
M. pneumoniae	33	30 (90.9%)	39	38 (97.4%)

15 REFERENCES

1. Clinical and Laboratory Standards Institute (CLSI). Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard - Tenth Edition. CLSI document M07-A10, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2015.
2. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Sixth Informational Supplement. CLSI document M100-S26, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2016.
3. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Disk Diffusion Susceptibility Tests; Approved Standard – Twelfth Edition. CLSI document M02-A12, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2015.
4. Clinical and Laboratory Standards Institute (CLSI). Methods for Antimicrobial Dilution and Disk Susceptibility Testing for Infrequently Isolated or Fastidious Bacteria: Approved Guidelines—Third Edition. CLSI document M45-A3, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2016.

16 HOW SUPPLIED/STORAGE AND HANDLING

Zithromax SD is supplied in bottles containing 2 g of azithromycin and should be constituted with 60 mL of water.

Storage
Before constitution, store dry powder at or below **30°C (86°F)**.

After constitution, store suspension at **25°C (77°F)**; excursions permitted to **15-30°C (59-86°F)** [see USP Controlled Room Temperature]. Do not refrigerate or freeze.

Constituted suspension should be consumed within 12 hr. For adult patients, the entire bottle should be consumed. For pediatric patients, any suspension remaining after dosing **MUST** be discarded.

17 PATIENT COUNSELING INFORMATION

General Patient Counseling

- Patients should be instructed to take Zithromax SD on an empty stomach (at least 1 hr before or 2 hr following a meal).
- Patients should be told that Zithromax SD needs time to work, so the patient may not feel better right away. If the patient's symptoms do not improve in a few days, the patient or their guardian should call their doctor.
- Patients should be instructed to immediately contact a physician if any signs of an allergic reaction occur.
- 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.
- Patients who vomit within the first hr should contact their health care provider about further treatment.
- Keep bottle tightly closed. Store at room temperature. Use within 12 hr of constitution. Shake bottle well before use. Adult patients should consume the entire contents of the bottle.
- Patients should be advised that Zithromax SD may be taken without regard to antacids containing magnesium hydroxide and/or aluminum hydroxide.

Patients should be counseled that antibacterial drugs including Zithromax SD should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). Not taking the complete prescribed dose 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 Zithromax SD or other antibacterial drugs in the future.

Rx only

Marketing Authorization Holder:

Pfizer Inc. New York, N.Y., U.S.A.

Manufactured, Packed and Released By:

Pfizer Pharmaceuticals LLC
Vega Baja, Puerto Rico

Patient Information
Zithromax SD® (azithromycin extended release)
Oral suspension

Read the Patient Information that comes with Zithromax SD carefully before you take it. This leaflet does not take the place of talking with your doctor about you or your child's medical condition or treatment. Only your doctor can decide if Zithromax SD is right for you.

What is Zithromax SD?

Zithromax SD is an antibiotic that kills certain bacteria. Zithromax SD is dosed differently from other antibiotics.

You take **just one dose, one time**.

- Day 1: Take Zithromax SD in one dose. Zithromax SD starts working.
- Days 2 – 3: As with most antibiotics, you may not feel better right away.
- After Day 3: Zithromax SD continues to work over time. If your symptoms are not better, call your doctor.

Zithromax SD is used in adults against bacteria to treat certain kinds of pneumonia (lung infections)

Zithromax SD is used in adults against bacteria to treat sinus infections.

Zithromax SD only works against bacteria. It does not work against viruses, like the common cold or flu.

Who should not take Zithromax SD?

- You should not take Zithromax SD if allergic to:
  - anything in Zithromax SD. See the end of this leaflet for a complete list of ingredients in Zithromax SD.
  - antibiotics like erythromycin or telithromycin (Ketek®).

Talk with your doctor or pharmacist if you have questions about your medicine allergies.

Before you start Zithromax SD…

Tell your doctor about all your medical problems including if you:

- have liver problems.
- have kidney problems.
- have myasthenia gravis.
- are pregnant, or might be pregnant. It is not known if Zithromax SD could harm your baby.
- are breast-feeding.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements. Especially tell your doctor if you are taking warfarin (Coumadin®, Jantoven)

Know the medicines you take. Keep a list of your medicines and show it to your doctor or pharmacist when you get a new prescription.

Do I need to prepare Zithromax SD?

- If you get Zithromax SD in **liquid form, it is ready to take.**
- If you get Zithromax SD as **dry powder, you must add water to the bottle**
- **before you take it.** To prepare Zithromax SD:
    1. Open the bottle: To open the bottle, press down on the cap and twist.
    2. Use a measuring cup to add 60 mL (1/4 cup) water to the Zithromax SD bottle.
    3. Tightly close the bottle and shake to mix it.

How do I take Zithromax SD?

- Keep Zithromax SD at room temperature between 59ºF to 86ºF (15º to 30ºC).
- Shake the bottle well before using.
- Take Zithromax SD within 12 hr after it has been prepared by the pharmacy or you add water to the powder.
- Take Zithromax SD exactly how your doctor prescribes it. This will help to treat your infection and decrease the chance that Zithromax SD or other antibiotics will not work to treat infections in the future.
- Take all the medicine in the bottle.
- Take Zithromax SD on an empty stomach (at least 1 hr before eating or 2 hr after eating).
- You can take antacids with Zithromax SD.
- If you throw up (vomits) within one hr of taking Zithromax SD, call your doctor right away to see if more medicine is needed.

How will I know Zithromax SD is working?

Zithromax SD needs time to work, so you may not feel better right away. If your symptoms do not get better in a few days, call your doctor.

What are the possible side effects of Zithromax SD?

Zithromax SD may cause serious side effects. These happened in a small number of patients. Call your doctor right away or get emergency treatment if you have any of the following:

- **Serious allergic reaction or serious skin reaction:** Get emergency help right away if you have:
    - Skin rash (hives), sores in your mouth, or your skin blisters and peels
    - Trouble swallowing,
    - Swelling of your face, eyes, lips, tongue or throat
    - Wheezing or trouble breathing
    - New onset of fever and swollen lymph nodes

These symptoms could go away and then come back.

- **Diarrhea:** Call your doctor right away if you have diarrhea that does not go away, is severe, watery, or has blood in it. Diarrhea can occur as late as two or more months after you take an antibiotic such as Zithromax SD.
- **Abnormal heart rhythm.** Tell your doctor right away if you feel your heart beating in your chest or an abnormal heart beat, get dizzy or faint. This has been seen with other antibiotics like Zithromax SD.

The most common side effects in **adults** are:

- Diarrhea/loose stools
- Nausea
- Stomach pain
- Headache
- Vomiting

Tell your doctor if you have any side effects that bother you, or that does not go away.
These are not all of the possible side effects with Zithromax SD. For a list of all reported side effects, ask your doctor or pharmacist.

General information about Zithromax SD
Doctors sometimes prescribe medicines for conditions that are not in the patient leaflets. Do not use Zithromax SD for anything other than what your doctor prescribed. Do not give it to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information leaflet is a summary of the most important information about Zithromax SD. For more information, talk with your doctor. You can ask your doctor or pharmacist for information about Zithromax SD that is written for healthcare professionals.

What is in Zithromax SD?
Active ingredient: azithromycin dihydrate
Inactive ingredients: glyceryl behenate, poloxamer 407, sucrose, sodium phosphate tribasic anhydrous, magnesium hydroxide, hydroxypropyl cellulose, xanthan gum, colloidal silicon dioxide, titanium dioxide, artificial cherry flavor, and artificial banana flavor.

Marketing Authorization Holder:
Pfizer Inc

Manufactured Packed and Released By:

Pfizer
Pharmaceuticals LLC, Vega Baja, PR 00693

Revised February 2017

To report any side effect(s):	
United Arab Emirates (UAE): Pharmacovigilance and Medical Device section P.O.Box: 1853 Tel: 80011111 Email : pv@moh.gov.ae Drug Department Ministry of Health & Prevention Dubai	**Kuwait:** Website: www.moh.gov.kw/kdfc/ P.O. BOX: 22575, SAFAT 13086 KUWAIT
Jordan: Website : www.jfda.jo Tel: 0096265632000 - 0096264602550 Fax:0096265105916 - 0096265105893 E-mail : info@jfda.jo	**Lebanon :** Website :www.moph.gov.lb

Qatar: Website: www.moph.gov.qa	**Oman:** Web site: www.moh.gov.om Tel: 0096824601044 Fax: 0096824602287 E-mail: mohphar@omantel.net.om
Iran: (www.fda.gov.ir)	