Azithromycin tablets are 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. Recommended dosages and durations of therapy in adult and pediatric patient populations vary in these indications. [see DOSAGE AND ADMINISTRATION (2.2)]

1 INDICATIONS AND USAGE
Azithromycin tablets can be taken with or without food. [see INDICATIONS AND USAGE (2.1) ADULT PATIENTS]

1.1 Adult Patients
- Acute bacterial exacerbations of chronic bronchitis 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 Chlamydia pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, or Streptococcus pneumoniae in patients appropriate for oral therapy.
- Pharyngitis/tonsillitis caused by Streptococcus pyogenes as an alternative to first-line therapy in individuals who cannot use first-line therapy.
- Uncomplicated skin and skin structure infections due to Staphylococcus aureus, Streptococcus pyogenes, or Streptococcus agalactiae.
- 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.

1.2 Pediatric Patients
[see USE IN SPECIFIC POPULATIONS (8.4) AND CLINICAL STUDIES (14.2)]
- Acute otitis media (<6 months of age) caused by Haemophilus influenzae, Moraxella catarrhalis, or Streptococcus pneumoniae.
- Community-acquired pneumonia (≤6 months of age) due to Chlamydia pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, or Streptococcus pneumoniae in patients appropriate for oral therapy.
- Pharyngitis/tonsillitis (≤2 years of age) caused by Streptococcus pyogenes as an alternative to first-line therapy in individuals who cannot use first-line therapy.

1.3 Limitations 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 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).

1.4 Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of azithromycin and other antibacterial drugs, 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 Adult Patients
[see INDICATIONS AND USAGE (1.1) AND CLINICAL PHARMACOLOGY (12.3)]

<table>
<thead>
<tr>
<th>Infection</th>
<th>Recommended Dose/Duration of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired pneumonia</td>
<td>500 mg as a single dose on Day 1, followed by 250 mg once daily on Days 2 through 5</td>
</tr>
<tr>
<td>Pharyngitis/tonsillitis</td>
<td>500 mg as a single dose on Day 1, followed by 250 mg once daily on Days 2 through 5</td>
</tr>
<tr>
<td>Acute bacterial exacerbations of chronic obstructive pulmonary disease</td>
<td>500 mg once daily for 3 days OR 500 mg as a single dose on Day 1, followed by 250 mg once daily on Days 2 through 5</td>
</tr>
<tr>
<td>Acute bacterial sinusitis</td>
<td>500 mg once daily for 3 days</td>
</tr>
<tr>
<td>Genital ulcer disease (chancroid)</td>
<td>One single 1 gram dose</td>
</tr>
<tr>
<td>Non-gonococcal urethritis and cervicitis</td>
<td>One single 1 gram dose</td>
</tr>
</tbody>
</table>

*DUE TO THE INDICATED ORGANISMS [see INDICATIONS AND USAGE (1.1)]

Azithromycin tablets can be taken with or without food.

2.2 Pediatric Patients

<table>
<thead>
<tr>
<th>Infection</th>
<th>Recommended Dose/Duration of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute otitis media (&lt;6 months of age)</td>
<td>30 mg/kg as a single dose or 10 mg/kg once daily for 3 days or 10 mg/kg as a single dose on Day 1 followed by 5 mg/kg/day on Days 2 through 5.</td>
</tr>
<tr>
<td>Acute bacterial sinusitis (≤6 months of age)</td>
<td>10 mg/kg as a single dose on Day 1 followed by 5 mg/kg once daily on Days 2 through 5.</td>
</tr>
<tr>
<td>Community-acquired pneumonia (≤6 months of age)</td>
<td>30 mg/kg once daily for 3 days</td>
</tr>
<tr>
<td>Pharyngitis/tonsillitis (≤6 months of age)</td>
<td>10 mg/kg as a single dose on Day 1 followed by 5 mg/kg once daily on Days 2 through 5.</td>
</tr>
</tbody>
</table>

*DUE TO THE INDICATED ORGANISMS [see INDICATIONS AND USAGE (1.2)]

1 see dosage tables below for maximum doses evaluated by indication.
Azithromycin for oral suspension can be taken with or without food.

### PEDIATRIC DOSAGE GUIDELINES FOR OTITIS MEDIA, ACUTE BACTERIAL SINUSITIS, AND COMMUNITY-ACQUIRED PNEUMONIA (Age 6 months and above, [see USE IN SPECIFIC POPULATIONS (8.4)]) Based on Body Weight

#### OTITIS MEDIA AND COMMUNITY-ACQUIRED PNEUMONIA: (5-Day Regimen)*

<table>
<thead>
<tr>
<th>Weight</th>
<th>100 mg/5 mL</th>
<th>200 mg/5 mL</th>
<th>Total mL per Treatment Course</th>
<th>Total mg per Treatment Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kg</td>
<td>Day 1</td>
<td>Days 2 to 5</td>
<td>Day 1</td>
<td>Days 2 to 5</td>
</tr>
<tr>
<td>5</td>
<td>2.5 mL (1 tsp)</td>
<td>1.25 mL (½ tsp)</td>
<td>7.5 mL</td>
<td>150 mg</td>
</tr>
<tr>
<td>10</td>
<td>5 mL (1 tsp)</td>
<td>2.5 mL (½ tsp)</td>
<td>15 mL</td>
<td>300 mg</td>
</tr>
<tr>
<td>20</td>
<td>7.5 mL (1½ tsp)</td>
<td>3.75 mL (¾ tsp)</td>
<td>22.5 mL</td>
<td>600 mg</td>
</tr>
<tr>
<td>30</td>
<td>10 mL (2 tsp)</td>
<td>5 mL (1 tsp)</td>
<td>30 mL</td>
<td>600 mg</td>
</tr>
<tr>
<td>40</td>
<td>12.5 mL (2 ½ tsp)</td>
<td>6.25 mL (¾ tsp)</td>
<td>37.5 mL</td>
<td>1500 mg</td>
</tr>
<tr>
<td>50 and above</td>
<td>15 mL (3 tsp)</td>
<td>7.5 mL (1½ tsp)</td>
<td>50 mL</td>
<td>2000 mg</td>
</tr>
</tbody>
</table>

* 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)*

<table>
<thead>
<tr>
<th>Weight</th>
<th>100 mg/5 mL</th>
<th>200 mg/5 mL</th>
<th>Total mL per Treatment Course</th>
<th>Total mg per Treatment Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kg</td>
<td>Day 1</td>
<td>Days 1 to 3</td>
<td>Day 1</td>
<td>Days 1 to 3</td>
</tr>
<tr>
<td>5</td>
<td>2.5 mL (1 tsp)</td>
<td>7.5 mL</td>
<td>150 mg</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>5 mL (1 tsp)</td>
<td>15 mL</td>
<td>300 mg</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>7.5 mL (1½ tsp)</td>
<td>22.5 mL</td>
<td>900 mg</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>10 mL (2 tsp)</td>
<td>30 mL</td>
<td>1200 mg</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>12.5 mL (2 ½ tsp)</td>
<td>37.5 mL</td>
<td>1500 mg</td>
<td></td>
</tr>
<tr>
<td>50 and above</td>
<td>15 mL (3 tsp)</td>
<td>7.5 mL (1½ tsp)</td>
<td>50 mL</td>
<td>2000 mg</td>
</tr>
</tbody>
</table>

* Effectiveness of the 3-day or 1-day regimen in pediatric patients with acute bacterial sinusitis has not been established.

#### OTITIS MEDIA: (1-Day Regimen)

<table>
<thead>
<tr>
<th>Weight</th>
<th>200 mg/5 mL</th>
<th>Total mL per Treatment Course</th>
<th>Total mg per Treatment Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kg</td>
<td>1-Day Regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3.75 mL (¾ tsp)</td>
<td>3.75 mL</td>
<td>150 mg</td>
</tr>
<tr>
<td>10</td>
<td>7.5 mL (1½ tsp)</td>
<td>7.5 mL</td>
<td>300 mg</td>
</tr>
<tr>
<td>20</td>
<td>15 mL (3 tsp)</td>
<td>15 mL</td>
<td>600 mg</td>
</tr>
<tr>
<td>30</td>
<td>22.5 mL (4½ tsp)</td>
<td>22.5 mL</td>
<td>900 mg</td>
</tr>
<tr>
<td>40</td>
<td>30 mL (6 tsp)</td>
<td>30 mL</td>
<td>1200 mg</td>
</tr>
<tr>
<td>50 and above</td>
<td>37.5 mL (7½ tsp)</td>
<td>37.5 mL</td>
<td>1500 mg</td>
</tr>
</tbody>
</table>

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, 8 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 USE IN SPECIFIC POPULATIONS (8.4)]) Based on Body Weight

#### PHARYNGITIS/TONSILLITIS: (5-Day Regimen)

<table>
<thead>
<tr>
<th>Weight</th>
<th>200 mg/5 mL</th>
<th>Total mL per Treatment Course</th>
<th>Total mg per Treatment Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kg</td>
<td>Day 1 to 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2.5 mL (1 tsp)</td>
<td>12.5 mL</td>
<td>500 mg</td>
</tr>
<tr>
<td>17</td>
<td>5 mL (1 tsp)</td>
<td>25 mL</td>
<td>1000 mg</td>
</tr>
<tr>
<td>25</td>
<td>7.5 mL (1½ tsp)</td>
<td>37.5 mL</td>
<td>1500 mg</td>
</tr>
<tr>
<td>33</td>
<td>10 mL (2 tsp)</td>
<td>50 mL</td>
<td>2000 mg</td>
</tr>
<tr>
<td>40</td>
<td>12.5 mL (2 ½ tsp)</td>
<td>62.5 mL</td>
<td>2500 mg</td>
</tr>
</tbody>
</table>

Constituting instructions for azithromycin oral suspension: 300, 600, 900, 1200 mg bottles. The table below indicates the volume of water to be used for constitution:

<table>
<thead>
<tr>
<th>Amount of water to be added</th>
<th>Total volume after constitution (azithromycin content)</th>
<th>Azithromycin concentration after constitution</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 mL (300 mg)</td>
<td>15 mL (300 mg)</td>
<td>100 mg/mL</td>
</tr>
<tr>
<td>9 mL (600 mg)</td>
<td>15 mL (600 mg)</td>
<td>200 mg/mL</td>
</tr>
<tr>
<td>12 mL (900 mg)</td>
<td>22.5 mL (900 mg)</td>
<td>200 mg/mL</td>
</tr>
<tr>
<td>15 mL (1200 mg)</td>
<td>30 mL (1200 mg)</td>
<td>200 mg/mL</td>
</tr>
</tbody>
</table>

Shake well before each use. Oversized bottle provides shake space. Keep tightly closed.

After mixing, store suspension at 5° to 30°C (41° to 86°F) and use within 10 days. Discard after full dosing is completed.

### 3 DOSAGE FORMS AND STRENGTHS

**Azithromycin Tablets:** 250 mg are supplied as pink, oval shaped film-coated tablets, engraved with “LU” on one side and “L11” on the other side containing azithromycin monohydrate USP equivalent to 250 mg of azithromycin USP.

**Azithromycin Tablets:** 500 mg are supplied as pink, oval shaped film-coated tablets, engraved with “LU” on one side and “L12” on the other side containing azithromycin monohydrate USP equivalent to 500 mg of azithromycin USP.

### 4 CONTRAINDICATIONS

#### 4.1 Hypersensitivity

Azithromycin is contraindicated in patients with known hypersensitivity to azithromycin, erythromycin, any macrolide or lincosamide drug.

#### 4.2 Hepatic Dysfunction

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

### 5 WARNINGS AND PRECAUTIONS
5.1 Hypersensitivity
Serious allergic reactions, including angioedema, anaphylaxis, and dermatologic reactions including Acute Generalized Exanthematous Pustulosis (AGEP), Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported in patients on azithromycin therapy. [see CONTRAINDICATIONS (4.1)]

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 prolonged exposure to antigen is presently unknown.

If an allergic reaction occurs, the drug should be discontinued and appropriate therapy should be instituted. Physicians should be aware that allergic symptoms may reappear when symptomatic therapy has been 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 Infantile Hypertrophic Pyloric Stenosis (IHPS)
Following the use of azithromycin in neonates (treatment up to 42 days of life), IHPS has been reported. Direct parents and caregivers to contact their physician if vomiting or irritability with feeding occurs.

5.4 QT Prolongation
Prolonged cardiac repolarization and QT interval, imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen with 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, bradycardia, or uncorrected hypocalcemia or uncompensated heart failure
- patients on drugs known to prolong the QT interval
- patients with ongoing proarrhythmic conditions such as uncontrolled 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.

5.5 Clindamycin-Associated Diarrhea
Clindamycin-resistant associated diarrea 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 antibiotic therapy and may require colectomy. CDAD must be considered in any patient 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.

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

5.7 Use in Sexually Transmitted Disease
Azithromycin, at the recommended dose, should not be relied upon to treat syphilis. Antibacterial agents used 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 testing for gonorrhea performed at the time of diagnosis. Appropriate antibacterial therapy and follow-up tests for these diseases should be initiated if infection is confirmed.

5.8 Development of Drug-Resistant Bacteria
Prescribing azithromycin 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.

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 adverse reactions of angioedema and cholestatic jaundice were reported. 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 adverse reactions. In adults given 500 mg/day for 5 days, the discontinuation rate due to treatment-related adverse reactions was 0.6%. In clinical trials in pediatric patients given 30 mg/kg, either as a single dose or over 3 days, discontinuation because of adverse reactions was approximately 1%. Most of the adverse reactions leading to discontinuation were related to the gastrointestinal tract, e.g., nausea, vomiting, diarrhea, or abdominal pain. [see CLINICAL STUDIES (6.2)]

Adolescents

Multiple-dose regimen:

Cardiovascular:

Dyspnea, hypertension, chest pain.

Gastrointestinal:

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

Genitourinary:

Cystitis, 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 adverse reactions 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.

Adverse reactions that occurred in patients on the single 1-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 adverse reactions in patients receiving a single 2-gram dose of azithromycin were related to the gastrointestinal system. Adverse reactions 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 adverse reactions in pediatric patients were comparable to those seen in adults, with different incidence rates for the dosage regimen recommended in pediatric patients.

Acute Otitis Media:

For the recommended total dosage regimen of 30 mg/kg, the most frequent adverse reactions (≥1%) attributed to treatment were diarrhea, abdominal pain, vomiting, nausea, and rash. [See DOSAGE AND ADMINISTRATION (2) and CLINICAL STUDIES (14.2)]

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

<table>
<thead>
<tr>
<th>Dosage Regimen</th>
<th>Diarrhea %</th>
<th>Abdominal Pain %</th>
<th>Vomiting %</th>
<th>Nausea %</th>
<th>Rash %</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-day</td>
<td>4.3%</td>
<td>1.4%</td>
<td>4.5%</td>
<td>1.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>3-day</td>
<td>2.6%</td>
<td>1.7%</td>
<td>2.3%</td>
<td>0.4%</td>
<td>0.6%</td>
</tr>
<tr>
<td>5-day</td>
<td>1.8%</td>
<td>1.2%</td>
<td>1.1%</td>
<td>0.5%</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

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 adverse reactions attributed to treatment were diarrhea/loose stools, abdominal pain, vomiting, nausea, and rash.

The incidence is described in the table below:

<table>
<thead>
<tr>
<th>Dosage Regimen</th>
<th>Diarrhea/Loose stools %</th>
<th>Abdominal Pain %</th>
<th>Vomiting %</th>
<th>Nausea %</th>
<th>Rash %</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-day</td>
<td>5.8%</td>
<td>1.9%</td>
<td>1.9%</td>
<td>1.9%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

Pharyngitis/Tonsillitis:

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

The incidence is described in the table below:

<table>
<thead>
<tr>
<th>Dosage Regimen</th>
<th>Diarrhea %</th>
<th>Abdominal Pain %</th>
<th>Vomiting %</th>
<th>Nausea %</th>
<th>Rash %</th>
<th>Headache %</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-day</td>
<td>5.4%</td>
<td>3.4%</td>
<td>5.6%</td>
<td>1.8%</td>
<td>0.7%</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

With any of the treatment regimen, no other adverse reactions occurred in pediatric patients treated with azithromycin with a frequency greater than 1%. Adverse reactions 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 mucositis.

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, pharyngitis, pleural effusion, and rhinitis.

Skin and Appendages:

Eczema, fungal dermatitis, pruritus, sweating, urticaria, and vesiculobullous rash.

Special Senses:

Couspunctitis.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of azithromycin. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

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

Cardiovascular:

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 reports of tongue discoloration.

General:

Arthralgia, edema, urticaria, and angioedema.

Cardiovascular:

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 reports of tongue discoloration.

General:

Arthralgia, edema, urticaria, and angioedema.

Hematopoietic:

Thrombocytopenia.

Liver/Biliary:

Abnormal liver function, hepatitis, cholestatic jaundice, hepatic necrosis, and hepatic failure. [See WARNINGS AND PRECAUTIONS (5.2)]

Nervous System:

Couspuncturia, dizziness/vestigo, headache, somnolence, hyperactivity, nervousness, agitation, and syncope.

Psychiatric:
Clinical Considerations

Breastfeeding

Breastfeeding should be considered along with the mother's clinical need for azithromycin and any available data on the effects of azithromycin on milk production. The developmental and health benefits of breastfeeding for the infant must be weighed against any potential risks to the infant from azithromycin.

Risk Summary

8.2 Lactation

If the mother is breastfeeding or plans to breastfeed, azithromycin should be administered with caution. Available data from published literature and postmarketing experience over several decades with azithromycin use in pregnant women have not identified any drug-associated risks for major birth defects and miscarriage. However, azithromycin use in breastfeeding women should be carefully monitored while patients are receiving azithromycin and oral anticoagulants concomitantly.

Animal Data:

Azithromycin administered to pregnant rats, mice, and rabbits showed no drug-induced fetal malformations at doses up to 10, 20, and 80 mg/kg/day, respectively, based on body surface area. Decreased viability and delayed development were observed in the offspring of pregnant rats administered azithromycin from day 6 of pregnancy through weaning at a dose equivalent to 4 times an adult human daily dose of 500 mg based on body surface area.

Human Data:

Decreased viability, delayed developmental landmarks, and increased stress at parturition were observed in a pre-and postnatal study in pregnant rats administered azithromycin from day 6 of pregnancy through weaning at a dose equivalent to 4 times an adult human daily dose of 500 mg based on body surface area. These effects were not observed in a pre-and postnatal study in pregnant rats administered azithromycin from day 6 of pregnancy through weaning at a dose equivalent to 2 times an adult human daily dose of 500 mg based on body surface area.

The estimated background risk of major birth defects and miscarriage for the indicated populations is 2% to 4% and 15% to 20%, respectively. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.
Azithromycin is a macrolide antibacterial drug. [see Microbiology (12.4)]

11 DESCRIPTION
Azithromycin tablets USP contain the active ingredient azithromycin, a macroline antibacterial drug, for oral administration. Azithromycin has the chemical name C_{38}H_{72}N_{2}O_{12} and a molecular weight of 767.00.

Azithromycin is supplied as tablets containing azithromycin monohydrate equivalent to either 250 mg or 500 mg azithromycin and the following inactive ingredients: croscarmellose sodium, dibasic calcium phosphate, hydroxypropyl methyl cellulose, lactose monohydrate, magnesium stearate, sodium lauryl sulfate, titanium dioxide, triacetin and D&C Red #30.

Organic Impurities Test Pending.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Azithromycin is a macrolide antibacterial drug. [see Microbiology (12.4)]

12.2 Pharmacodynamics
Based on animal models of infection, the antibacterial activity of azithromycin appears to correlate with the ratio of area under the concentration-time curve to minimum inhibitory concentration (AUC/MIC) for certain pathogens (S. pneumoniae and S. aureus). The principal pharmacokinetic/pharmacodynamic parameter best associated with clinical and microbiological cure has not been elucidated in clinical trials with azithromycin.

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 oral azithromycin (500 mg, 1000 mg, and 1500 mg once daily). Co-administration of azithromycin increased the QTc interval dose- and concentration-dependent manner. In comparison to chloroquine alone, the maximum QTc (95% upper confidence bound) increases in QTc [mean (95% CI)] for 5 (10 mg), 7 (12 mg), and 9 (14 mg) with the co-administration of 500 mg, 1000 mg, and 1500 mg azithromycin, respectively.

12.3 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-∞} = 4.3 (1.2) mcg·hr/mL, C_{max} = 0.5 (0.2) mcg/mL, T_{max} = 2.2 (0.9) hours. Two azithromycin 250 mg tablets are bioequivalent to a single 500 mg tablet.

In a two-way crossover study, 12 adult healthy volunteers (6 males, 6 females) received 1500 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 of the fitted concentration profile was comparable between the 5-day and 3-day regimens.
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 Cmax by 23% but had no effect on AUC.
When azithromycin oral suspension was administered with food to 28 adult healthy male subjects, Cmax increased by 36% and AUC was unchanged.

Distribution
The serum protein binding of azithromycin is variable in the concentration range approximating human exposures, decreasing from 51% at 0.02 mcg/mL to 7% at 2 mcg/mL.
The antibacterial 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.
Azithromycin has been shown to penetrate into human tissues, including skin, lung, tongue, and cervix. Extensive tissue distribution was confirmed by examination of additional tissues and fluids (bone, ejaculate 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 significance of these tissue concentration data is unknown.
Following a regimen of 500 mg on the first day and 250 mg daily for 4 days, very low concentrations were noted in cerebrospinal fluid (less than 0.01 mcg/mL) in the presence of nonflamed meningitis.

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

Elimination
Plasma concentrations of azithromycin following single 500 mg oral and IV doses declined in a polyphasic pattern resulting in a mean apparent plasma clearance of 630 mL/min and terminal elimination half-life of 80 h. 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.

Specific Populations
Patients with Renal Impairment:
Azithromycin pharmacokinetics was 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 x 250 mg capsules), mean Cmax and AUC(0-24) increased by 5.1% and 4.2%, respectively, in subjects with mild to moderate renal impairment (GFR >30 to 60 mL/min) compared to subjects with normal renal function (GFR >60 mL/min). The mean Cmax and AUC(0-24) increased 61% and 35%, respectively, in subjects with severe renal impairment (GFR <10 mL/min) compared to subjects with normal renal function (GFR >60 mL/min).

Patients with Hepatic Impairment:
The pharmacokinetics of azithromycin in subjects with hepatic impairment has not been established.

Male and Female Patients:
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:
Pharmacokinetic parameters in older volunteers (65 to 85 years old) were similar to those in young adults (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 Geriatric Use [5])

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 in five groups of pediatric patients (aged 1 to 5 years and 5 to 17 years, respectively). The mean pharmacokinetic parameters on day 5 were Cmax = 0.216 mcg/mL, Tmax = 1.9 hr and AUC(0-24) = 1.822 mcg·hr/mL for the 1 to 5-year-old group and were Cmax = 0.383 mcg/mL, Tmax = 2.4 hr, and AUC(0-24) = 3.109 mcg·hr/mL for the 5 to 15-year-old group.
In another 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 azithromycin pharmacokinetics following a low fat breakfast. In this study, azithromycin concentrations were determined over a 24 hr period following the last daily dose. Patients weighing above 41.7 kg received the maximum adult daily dose of 500 mg. Seventeen patients (weighing 41.7 kg or less) 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)]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>12 mg/kg (5 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (mcg/mL)</td>
<td></td>
<td>0.5 (0.4)</td>
</tr>
<tr>
<td>Tmax (hr)</td>
<td></td>
<td>2.2 (0.8)</td>
</tr>
<tr>
<td>AUC(0-24) (mcg·hr/mL)</td>
<td>3.9 (1.9)</td>
<td></td>
</tr>
</tbody>
</table>

Single dose pharmacokinetics of azithromycin in pediatric patients given doses of 30 mg/kg have not been studied. (see DOSAGE AND ADMINISTRATION [2])

Drug Interaction Studies
Drug interaction studies were performed with azithromycin 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 1 and the effects of other drugs on the pharmacokinetics of azithromycin are shown in Table 2.

Co-administration 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 co-administered with azithromycin.

Co-administration of azithromycin with efavirenz or fluconazole had a modest effect on the pharmacokinetics of azithromycin. Nelfinavir significantly increased the Cmax and AUC of azithromycin. No dosage adjustment of azithromycin is recommended when administered with drugs listed in Table 2. (see DRUG INTERACTIONS [7,3])

<table>
<thead>
<tr>
<th>Drug Interactions: Pharmacokinetic Parameters for Co-administered Drugs in the Presence of Azithromycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-administered Drug</td>
</tr>
<tr>
<td>Atorvastatin</td>
</tr>
<tr>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Ceftriaxone</td>
</tr>
<tr>
<td>Diclofenac</td>
</tr>
<tr>
<td>Flavoxate</td>
</tr>
</tbody>
</table>

*Ratio (with/without azithromycin) of Co-administered Drug Pharmacokinetic Parameters (90% CI) No Effect = 1.00
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 clastogen assay, and mouse bone marrow clastogen assay. In fertility studies conducted in male and female rats, oral administration of azithromycin for 64 to 66 days (males) or 15 days (females) prior to and during cohabitation resulted in decreased pregnancy rate at 20 and 30 mg/kg/day when both males and females were treated with azithromycin. This minimal effect on pregnancy rate (approximately 12% reduction compared to concurrent controls) did not become more pronounced when the dose was increased from 20 to 30 mg/kg/day (approximately 0.4 to 0.6 times the adult daily dose of 500 mg based on body surface area) and it was not observed when only one animal in the mated pair was treated. There were no effects on any other reproductive parameters, and there were no effects on fertility at 10 mg/kg/day. The relevance of these findings to patients being treated with azithromycin at the doses and durations recommended in the prescribing information is uncertain.

13.2 Animal Toxicology and/or Pharmacology

The doses and durations recommended in the prescribing information is uncertain. The relevance of these findings to patients being treated with azithromycin at 500 mg based on body surface area) and it was not observed when only one animal in the mated pair was treated. There were no effects on any other reproductive parameters, and there were no effects on fertility at 10 mg/kg/day. The relevance of these findings to patients being treated with azithromycin at the doses and durations recommended in the prescribing information is uncertain.
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 and rats treated with azithromycin at doses which, expressed on the basis of body surface area, are similar to or less than the highest recommended adult human 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) at the observed maximal plasma concentration of 1.3 mcg/mL (1.6 times the observed Cmax of 0.821 mcg/mL at the adult dose of 2 g). Similarly, it has been shown in the dog (10 mg/kg/day) at the observed maximal serum concentration of 1 mcg/mL (1.2 times the observed Cmax of 0.821 mcg/mL at the adult dose of 2 g). Phospholipidosis was also observed in neonatal rats dosed for 10 days at 30 mg/kg/day, which is less than the pediatric dose of 60 mg/kg based on the surface area. It was not observed in neonatal rats treated for 10 days at 40 mg/kg/day with mean maximal serum concentration of 1.86 mcg/mL, approximately 1.5 times the Cmax 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 Cmax.

The significance of these findings for animals and for human is unknown.

### 14 CLINICAL STUDIES

#### 14.1 Adult Patients

**Acute Bacterial Exacerbations of Chronic Bronchitis**

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 Days 21 to 24. For the 304 patients analyzed in the modified intent-to-treat analysis at 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 Days 21 to 24 visit for the bacteriologically evaluable patients by pathogen:

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Azithromycin (3 Days)</th>
<th>Clarithromycin (10 Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pneumoniae</td>
<td>29/32 (91%)</td>
<td>21/27 (78%)</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>12/14 (86%)</td>
<td>14/16 (98%)</td>
</tr>
<tr>
<td>M. catarrhalis</td>
<td>11/12 (92%)</td>
<td>12/15 (83%)</td>
</tr>
</tbody>
</table>

**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 three times a day 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 304 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 10 visit, the clinical cure rate for 3 days of azithromycin was 85% (125/147) compared to 82% (129/157) for 10 days of clarithromycin.

**Acute Otitis Media**

Efficacy using azithromycin given over 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):

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Penicillin V</th>
<th>Azithromycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pyogenes</td>
<td>284/308 (93%)</td>
<td>287/308 (98%)</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>28/30 (93%)</td>
<td>28/30 (93%)</td>
</tr>
</tbody>
</table>

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

**Acute Otitis Media**

Efficacy using azithromycin given over 5 days (10 mg/kg on Day 1 followed by 5 mg/kg on Days 2 to 5):

**Trial 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.

**Trial 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.

**Acute Bacterial Exacerbations of Chronic Bronchitis**

Phospholipidosis 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 and rats treated with azithromycin at doses which, expressed on the basis of body surface area, are similar to or less than the highest recommended adult human 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) at the observed maximal plasma concentration of 1.3 mcg/mL (1.6 times the observed Cmax of 0.821 mcg/mL at the adult dose of 2 g). Similarily, it has been shown in the dog (10 mg/kg/day) at the observed maximal serum concentration of 1 mcg/mL (1.2 times the observed Cmax of 0.821 mcg/mL at the adult dose of 2 g). Phospholipidosis was also observed in neonatal rats dosed for 10 days at 30 mg/kg/day, which is less than the pediatric dose of 60 mg/kg based on the surface area. It was not observed in neonatal rats treated for 10 days at 40 mg/kg/day with mean maximal serum concentration of 1.86 mcg/mL, approximately 1.5 times the Cmax 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 Cmax.

The significance of these findings for animals and for human is unknown.
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/clavulanic acid (7:1) divided doses q12h for 10 days. Each patient received active drug and placebo matched for the comparator.

For the 362 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 Days 24 to 28 visit, the clinical success rate was 74% for azithromycin and 94% for the control agent.

**Efficacy using azithromycin 30 mg/kg given as a single dose:**

**Trial 4**

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 as a single dose on Day 1) or amoxicillin/clavulanic acid (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 (Days 12 to 16) and Test of Cure (Days 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 83% for the comparator. For the 365 subjects who were evaluated at Test of Cure, the clinical success rate was 75% for both azithromycin and the comparator.

**Trial 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 evaluated for clinical modified Intent-to-Treat (MITT) analysis, the clinical success rate (i.e., cure plus improvement) at Day 10 was 85% and for the 242 patients evaluated at Days 24 to 28, the clinical success rate (cure) was 85%.

### Presumed Bacteriologic Eradication

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Day 10</th>
<th>Days 24-28</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pneumonia</td>
<td>76/76 (92%)</td>
<td>67/76 (81%)</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>30/42 (71%)</td>
<td>28/44 (64%)</td>
</tr>
<tr>
<td>M. catarrhalis</td>
<td>10/10 (100%)</td>
<td>10/10 (100%)</td>
</tr>
<tr>
<td>Overall</td>
<td>110/128 (86%)</td>
<td>105/130 (81%)</td>
</tr>
</tbody>
</table>

**16 HOW SUPPLIED/STORAGE AND HANDLING**

Azithromycin tablets USP are supplied in the following strengths and package configurations:

- Azithromycin tablets USP, 250 mg are supplied as pink, oval shaped film-coated tablets, engraved with “LU” on one side and “L12” on the other side containing azithromycin monohydrate USP equivalent to 250 mg of azithromycin USP.
- These are packaged in bottles and blister cards as follows:
  - Bottles of 30 Tablets NDC 68180-160-06
  - Carton of 3 Blister Cards (6 Tablets per Blister Card) NDC 68180-160-13
- Azithromycin tablets USP, 500 mg are supplied as pink, oval shaped film-coated tablets, engraved with “LU” on one side and “L12” on the other side containing azithromycin monohydrate USP equivalent to 300 mg of azithromycin USP.
- These are packaged in bottles and blister cards as follows:
  - Bottles of 30 Tablets NDC 68180-161-06
  - Carton of 3 Blister Cards (3 Tablets per Blister Card) NDC 68180-161-13

Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F). [See USP Controlled Room Temperature].

**17 PATIENT COUNSELING INFORMATION**

Advise the patient to read the FDA-approved patient labeling (Patient Information).

### General Patient Counseling

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.

Direct parents or caregivers to contact their physician if vomiting and irritability with feeding occurs in the infant.

Patients should be counseled that antibacterial drugs including azithromycin should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When an antibacterial drug is 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 or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibacterials which usually ends when the antibacterial is discontinued. Sometimes after starting treatment with antibacterials patients can develop diarrhea 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 antibacterial drug. If this occurs, patients should contact their physician as soon as possible.
What are azithromycin tablets?

Azithromycin tablets are a macrolide antibiotic prescription medicine used in adults 18 years or older to treat certain infections caused by certain germs called bacteria. These bacterial infections include:

- acute worsening of chronic bronchitis
- acute sinus infection
- community-acquired pneumonia
- infected throat or tonsils
- skin infections
- infections of the urethra or cervix
- genital ulcers in men

Azithromycin tablets are also used in children to treat:

- ear infections
- community-acquired pneumonia
- infected throat or tonsils

Azithromycin should not be taken by people who cannot tolerate oral medications because they are very ill or have certain other risk factors including:

- have cystic fibrosis
- have hospital acquired infections
- have known or suspected bacteria in the blood
- need to be in the hospital
- are elderly

- have any medical problems that can lower the ability of the immune system to fight infections

Azithromycin tablets are not for viral infections such as the common cold.

It is not known if azithromycin tablets are safe and effective for genital ulcers in women.

It is not known if azithromycin tablets are safe and effective for children with ear infections, sinus infections, and community-acquired pneumonia under 6 months of age.

It is not known if azithromycin tablets are safe and effective for infected throat or tonsils in children under 2 years of age.

Who should not take azithromycin tablets?

Do not take azithromycin tablets if you:

- have had a severe allergic reaction to certain antibiotics known as macrolides or ketolides including azithromycin and erythromycin.
- have a history of cholestatic jaundice or hepatic dysfunction that happened with the use of azithromycin.

What should I tell my healthcare provider before taking azithromycin tablets?

Before you take azithromycin tablets, tell your healthcare provider if you:

- have pneumonia
- have cystic fibrosis
- have known or suspected bacteremia (bacterial infection in the blood)
- have liver or kidney problems
- have an irregular heartbeat, especially a problem called "QT prolongation"
- have a problem that causes muscle weakness (myasthenia gravis)
- have any other medical problems
- are pregnant or plan to become pregnant. It is not known if azithromycin tablets will harm your unborn baby.
- are breastfeeding or plan to breastfeed. Azithromycin has been reported to pass into breast milk.

Talk to your healthcare provider about the best way to feed your baby while you take azithromycin tablets.

Contact your healthcare provider immediately if you are giving azithromycin tablets to a young child (less than 6 weeks of age) and he or she vomits or becomes irritable when fed.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Azithromycin tablets and other medicines may affect each other causing side effects. Azithromycin tablets may affect the way other medicines work, and other medicines may affect how azithromycin tablets work.

Especially tell your healthcare provider if you take:

- statins
- a blood thinner (warfarin)
- digoxin
- colchicine
- phenytoin
- an antacid that contains aluminum or magnesium

Know the medicines you take. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take azithromycin tablets?

- Take azithromycin tablets exactly as your healthcare provider tells you to take it.
- Azithromycin tablets can be taken with or without food.
- Do not skip any doses of azithromycin tablets or stop taking it, even if you begin to feel better, until you finish your prescribed treatment unless you have a serious allergic reaction or your healthcare provider tells you to stop taking azithromycin tablets. "See What are the possible side effects of azithromycin tablets?" If you skip doses, or do not complete the total course of azithromycin tablets your treatment may not work as well and your infection may be harder to treat. Taking all of your azithromycin tablets will help lower the chance that the bacteria will become resistant to azithromycin tablets.
- If the bacteria becomes resistant to azithromycin, azithromycin tablets and other antibiotic medicines may not work for you in the future.
- If you take too much azithromycin tablets, call your healthcare provider or get medical help right away.

What are the possible side effects of azithromycin tablets?

Azithromycin tablets can cause serious side effects, including:

- Serious allergic reactions. Allergic reactions can happen in people taking azithromycin tablets the active ingredient in azithromycin tablets, even after only 1 dose. Stop taking azithromycin tablets and get emergency medical help right away if you have any of the following symptoms of a severe allergic reaction:
  - trouble breathing or swallowing
  - swelling of the lips, tongue, face
• Throat tightness, hoarseness
• Rapid heartbeat
• Faintness
• New onset of fever and swollen lymph nodes

Stop taking azithromycin tablets at the first sign of a skin rash and call your healthcare provider.

Skin rash may be a sign of a more serious reaction to azithromycin tablets.

• Liver damage (hepatotoxicity). Hepatotoxicity can happen in people who take azithromycin tablets.

Call your healthcare provider right away if you have unexplained symptoms such as:

• Nausea or vomiting
• Stomach pain
• Fever
• Weakness
• Abdominal pain or tenderness
• Itching
• Unusual tiredness
• Loss of appetite
• Change in the color of your bowel movements
• Dark colored urine
• Yellowing of your skin or of the whites of your eyes

Stop taking azithromycin tablets and tell your healthcare provider right away if you have yellowing of your skin or white part of your eyes, or if you have dark urine. These can be signs of a serious reaction to azithromycin tablets (a liver problem).

• Serious heart rhythm changes (QT prolongation and torsades de pointes).

Tell your healthcare provider right away if you have a change in your heartbeat (a fast or irregular heartbeat), or if you feel faint and dizzy. Azithromycin tablets may cause a rare heart problem known as prolongation of the QT interval. This condition can cause an abnormal heartbeat and can be very dangerous. The chances of this happening are higher in people:

• Who are elderly
• With a family history of prolonged QT interval
• With low blood potassium
• Who take certain medicines to control heart rhythm (antiarrhythmics)

• Worsening of myasthenia gravis (a problem that causes muscle weakness).

Certain antibiotics like azithromycin tablets may cause worsening of myasthenia gravis symptoms, including muscle weakness and breathing problems. Call your healthcare provider right away if you have any worsening muscle weakness or breathing problem.

• Diarrhea. Tell your healthcare provider right away if you have watery diarrhea, diarrhea that does not go away, or bloody stools. You may experience cramping and a fever. This could happen after you have finished your azithromycin tablets.

The most common side effects of azithromycin tablets include:

• Nausea
• Stomach pain
• Vomiting

These are not all the possible side effects of azithromycin tablets. Tell your healthcare provider about any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store azithromycin tablets?

Store azithromycin tablets at 15° to 30°C (59° to 86°F).

Safely throw away any medicine that is out of date or no longer needed.

Keep azithromycin tablets and all medicines out of the reach of children.

General information about the safe and effective use of azithromycin tablets.

Medicines are sometimes prescribed for purposes other than those listed in the Patient Information leaflet. Do not use azithromycin tablets for a condition for which it was not prescribed. Do not give azithromycin tablets to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information leaflet summarizes the most important information about azithromycin tablets. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about azithromycin tablets that is written for health professionals.

For more information, go to www.lupinpharmaceuticals.com or call 1-800-399-2561.

What are the ingredients in azithromycin tablets?

Azithromycin Tablets:

Active ingredient: azithromycin monohydrate

Inactive ingredients: croscarmellose sodium, dibasic calcium phosphate, hydroxypropyl methyl cellulose, lactose monohydrate, magnesium stearate, sodium lauryl sulfate, titanium dioxide, triacetin and D & C Red #30.

How to open the blister:
This Patient Information has been approved by the U.S. Food and Drug Administration.

Manufactured for:
Lupin Pharmaceuticals, Inc.
Baltimore, Maryland 21202
United States
Manufactured by:
Lupin Limited
Goa - 403722
India
Revised: July 2019
ID#: 260769

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL
Azithromycin Tablets USP, 250 mg
Container Label-30 Tablets
NDC 68180-160-06

Azithromycin Tablets USP, 250 mg
3 Card x 6 Tablets- Outer Carton Label
NDC 68180-160-13

Azithromycin Tablets USP, 250 mg
6 Tablets- Blister Card
NDC 68180-160-11
# AZITHROMYCIN MONOHYDRATE

**azithromycin monohydrate tablet**

## Product Information

<table>
<thead>
<tr>
<th>Product Type</th>
<th>Item Code (Source)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HUMAN PRESCRIPTION DRUG</td>
<td>NDC:68180-160-01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Route of Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORAL</td>
</tr>
</tbody>
</table>

## Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZITHROMYCIN MONOHYDRATE (UNII: JTE4MNN1MD)</td>
<td>(AZITHROMYCIN ANHYDROUS - UNII:J2KLZ20U1M)</td>
<td>AZITHROMYCIN ANHYDROUS 250 mg</td>
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</table>

## Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>CALCIUM PHOSPHATE, DIBASIC, ANHYDROUS (UNII:L11K75P92J)</td>
<td></td>
</tr>
<tr>
<td>CROSCARMELLOSE SODIUM (UNII:MS015R4885)</td>
<td></td>
</tr>
<tr>
<td>D&amp;C RED NO. 30 (UNII:2S42T2808B)</td>
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</tr>
<tr>
<td>HYPROMELLOSE 2910 (15 MPA.S) (UNII:36SFW2JZ0W)</td>
<td></td>
</tr>
<tr>
<td>LACTOSE MONOHYDRATE (UNII:EWQ57Q8I5X)</td>
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</tr>
<tr>
<td>MAGNESIUM STEARATE (UNII:70097M6I30)</td>
<td></td>
</tr>
<tr>
<td>SODIUM LAURYL SULFATE (UNII:368GB5141J)</td>
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</tr>
<tr>
<td>TITANIUM DIOXIDE (UNII:15FIX9V2JP)</td>
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</tr>
<tr>
<td>TRIACTIN (UNII:MXQ2C36M79)</td>
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</tr>
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</table>

## Product Characteristics

<table>
<thead>
<tr>
<th>Color</th>
<th>Shape</th>
<th>Size</th>
<th>Imprint Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>PINK</td>
<td>OVAL</td>
<td>14mm</td>
<td>LU;L11</td>
</tr>
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</table>

## Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:68180-160-13</td>
<td>3 in 1 CARTON</td>
<td>08/18/2015</td>
<td>08/18/2015</td>
</tr>
<tr>
<td>2</td>
<td>NDC:68180-160-06</td>
<td>30 in 1 CONTAINER; Type 0: Not a Combination Product</td>
<td>08/18/2015</td>
<td>08/18/2015</td>
</tr>
</tbody>
</table>

## Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANDA</td>
<td>ANDA065398</td>
<td>08/18/2015</td>
<td></td>
</tr>
</tbody>
</table>
# AZITHROMYCIN MONOHYDRATE

## Product Information

**Product Type:** HUMAN PRESCRIPTION DRUG  
**Item Code (Source):** NDC:68180-161-61  
**Route of Administration:** ORAL

## Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZITHROMYCIN MONOHYDRATE</td>
<td>(UNII: JTE4MNN1MD)</td>
<td>500 mg</td>
</tr>
<tr>
<td>AZITHROMYCIN ANHYDROUS</td>
<td>(UNII: J2KLZ20U1M)</td>
<td></td>
</tr>
</tbody>
</table>

## Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>CALCIUM PHOSPHATE, DIBASIC, ANHYDROUS</td>
<td>(UNII: L11K75P92J)</td>
</tr>
<tr>
<td>CROSCARMELLOSE SODIUM</td>
<td>(UNII: M28OL1HH48)</td>
</tr>
<tr>
<td>HYPROELLOSE 210 (15 MPA.S)</td>
<td>(UNII: 36459U2JNO)</td>
</tr>
<tr>
<td>LACTOSE MONOHYDRATE</td>
<td>(UNII: ENQW9H6G)</td>
</tr>
<tr>
<td>MAGNESIUM STEARATE</td>
<td>(UNII: 17G8I7E68A)</td>
</tr>
<tr>
<td>SODIUM LACTATE</td>
<td>(UNII: 16BB3G6T01)</td>
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<tr>
<td>TITANIUM DIOXIDE</td>
<td>(UNII: 1S5J455536)</td>
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<tr>
<td>TRIACETIN</td>
<td>(UNII: XHX3C3X673)</td>
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## Product Characteristics

- **Color:** Pink
- **Shape:** Oval
- **Size:** 17mm
- **Flavor:** Imprint Code: LU;L12
- **Contains:**

## Packaging

<table>
<thead>
<tr>
<th># Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 68180-161-13</td>
<td>3 in 1 CARTON</td>
<td>08/18/2015</td>
<td></td>
</tr>
<tr>
<td>1 68180-161-06</td>
<td>3 in 1 BLISTER PACK; Type: Not a Combination Product</td>
<td>08/18/2015</td>
<td></td>
</tr>
<tr>
<td>2 68180-161-06</td>
<td>30 in 1 CONTAINER; Type: Not a Combination Product</td>
<td>08/18/2015</td>
<td></td>
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</tbody>
</table>

## Marketing Information

- **Marketing Category:** ANDA  
- **Application Number or Monograph Citation:** ANDA065399  
- **Marketing Start Date:** 08/18/2015  
- **Marketing End Date:** |

## Labeler

- **Labeler:** Lupin Pharmaceuticals, Inc. (089153071)

## Registrant

- **Registrant:** LUPIN LIMITED (675923163)

## Establishment

- **Name:** LUPIN LIMITED  
- **Address:** 677600414  
- **Business Operations:** MANUFACTURE(68180-160, 68180-161), PACK(68180-160, 68180-161)

Revised: 7/2019  
Lupin Pharmaceuticals, Inc.