CASE:

FZX, a 41 year old white female, is seen in the outpatient department for complaints of low grade fever, cough, and mild respiratory distress. CXR shows light, patchy infiltrates. The attending physician suspects mycoplasma pneumonia and wishes to treat the patient with erythromycin. However, before writing a prescription, she seeks your advice. She explains that she has heard a lot lately from the pharmaceutical company representatives about the “new erythromycins” and asks for your appraisal and advice in selecting appropriate macrolide therapy for this patient.

QUESTIONS TO ADDRESS:

1. What are the differences between the three major macrolides (erythromycin, clarithromycin and azithromycin) in terms of spectrum of antibacterial activity?
2. Are there important pharmacokinetic properties which distinguish one macrolide from another? If so, what are they?
3. Are there important differences in side effect profiles that help distinguish between the various macrolides?
4. Are there important drug interactions to avoid with erythromycin? Do these interactions, or others, occur with the other macrolides?
5. Based upon the above discussion, are there differences in clinical indications of the various macrolides of which the pharmacist should be aware?
**Structures of Macrolides**

- Azithromycin
- Clarithromycin
- Erythromycin

**Mechanism of Action**

- Bind to 50S subunit of ribosomes causing them to dissociate from the mRNA resulting in premature termination of the amino acid chain & cessation of protein synthesis

**Microbiologic Activity of Macrolides**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Erythromycin</th>
<th>Azithromycin</th>
<th>Clarithromycin</th>
<th>Dihithromycin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gram-Positive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. aureus (50S)</td>
<td>0.12/0.128</td>
<td>0.12/0.128</td>
<td>0.06/0.128</td>
<td>0.25/0.128</td>
</tr>
<tr>
<td>S. aureus (30S)</td>
<td>&gt;0.128</td>
<td>&gt;0.128</td>
<td>&gt;0.128</td>
<td>&gt;0.128</td>
</tr>
<tr>
<td>S. pyogenes</td>
<td>0.03/0.128</td>
<td>0.06/0.128</td>
<td>0.015/0.5</td>
<td>0.1/0.128</td>
</tr>
<tr>
<td>Streptococcus spp.</td>
<td>0.2/0.128</td>
<td>2/0.128</td>
<td>0.5/0.128</td>
<td>1/0.128</td>
</tr>
<tr>
<td><strong>Gram-Negative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. catarrhalis</td>
<td>0.12/2</td>
<td>&lt;0.015/0.12</td>
<td>0.061</td>
<td>0.12/0.25</td>
</tr>
<tr>
<td>N. gonorrhoeae</td>
<td>0.12/2</td>
<td>&lt;0.025/0.25</td>
<td>0.125/2</td>
<td>2/4</td>
</tr>
<tr>
<td>L. pneumophila</td>
<td>0.05/2</td>
<td>0.5/2</td>
<td>0.125/2.5</td>
<td>4/16</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>0.025</td>
<td>0.25/4</td>
<td>0.16</td>
<td>0.8</td>
</tr>
</tbody>
</table>

*literature-derived means

**Microbiologic Activity of Macrolides**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Erythromycin</th>
<th>Azithromycin</th>
<th>Clarithromycin</th>
<th>Dihithromycin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anaerobes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. fusiformis</td>
<td>0.04/2</td>
<td>0.01/NA</td>
<td>0.004/0.125</td>
<td>0.004/0.125</td>
</tr>
<tr>
<td>C. perfringens</td>
<td>0.12/0.25</td>
<td>0.25/0.25</td>
<td>0.03/0.03</td>
<td>2/2</td>
</tr>
<tr>
<td>P. acnes</td>
<td>&gt;0.01</td>
<td>&gt;0.004/0.03</td>
<td>&gt;0.01/0.03</td>
<td>0.25/0.5</td>
</tr>
</tbody>
</table>

*literature-derived means
Streptococcus pneumoniae
Macrolide Resistance

• *erm B*
  – Methylation of 23S rRNA
  – High level macrolide resistance (MICs ≥ 64)
  – Prevalence (in USA) ≈ 25%

• *mef A*
  – Efflux pump
  – Mid-range macrolide resistance (MICs 1 to 32)
  – Prevalence (in USA) ≈ 75%

Macrolide MIC Frequency Distributions for *S. pneumoniae* (n = 1531), 1999-2000

ERYTHROMYCIN

Macrolide MIC Frequency Distributions Versus *Streptococcus pneumoniae* (n = 1531), 1999-2000

CLARITHROMYCIN

AZITHROMYCIN

G. Doern. Personal Communication.
Macrolides and Related Antibiotics
John A. Bosso, Pharm.D.

**Erythromycin-resistant *S. pneumoniae* 1999-2000**

- Lower respiratory tract (177/811, 26.0%)
- Middle ear fluid (54/185, 35.4%)
- Sinus (17/48, 35.4%)
- Other upper respiratory (5/173, 28.5%)

*Total number of isolates, n = 1531

**Streptococcus pneumoniae, 1999-2000**

- 0 - 5 years (148/447, 33.1%)
- 6 - 20 years (26/87, 32.2%)
- 21 - 64 years (145/643, 22.6%)
- ≥65 years (78/339, 23.0%)

*Total number of isolates, n = 1531

---

**Erythromycin Salts**

- **Base**
  - Inactivated by acid; absorption delayed by food
- **Stearate**
  - More acid stable; absorption decreased by food
- **Estolate**
  - Acid stable; absorption not affected by food

---

**Erythromycin Salts**

- **Ethylsuccinate**
  - Acid stable; absorption delayed by food
- **Lactobionate**
  - IV form
Macrolides and Related Antibiotics
John A. Bosso, Pharm.D.

### Pharmacokinetics of Macrolides

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Dose (mg)</th>
<th>Cmax (µg/mL)</th>
<th>tmax (h)</th>
<th>AUC (µg*h/L)</th>
<th>V (L/kg)</th>
<th>Protein Binding (%)</th>
<th>Tissue Conc (µg/kg)</th>
<th>t1/2 (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dirithromycin</td>
<td>500 ad</td>
<td>0.8</td>
<td>2-3</td>
<td>10-15</td>
<td>10-15</td>
<td>5-10</td>
<td>5-10</td>
<td>5-10</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>500 bid</td>
<td>3.6</td>
<td>1.6-1.7</td>
<td>10-15</td>
<td>10-15</td>
<td>5-10</td>
<td>5-10</td>
<td>5-10</td>
</tr>
<tr>
<td>Clarithromycin IR</td>
<td>500 bid</td>
<td>2.4-3.5</td>
<td>2-2.5</td>
<td>10-15</td>
<td>10-15</td>
<td>5-10</td>
<td>5-10</td>
<td>5-10</td>
</tr>
<tr>
<td>Clarithromycin ER</td>
<td>1000 ad</td>
<td>2.5</td>
<td>0.5-1.5</td>
<td>10-15</td>
<td>10-15</td>
<td>5-10</td>
<td>5-10</td>
<td>5-10</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>500 ad</td>
<td>0.62</td>
<td>2-4</td>
<td>10-15</td>
<td>10-15</td>
<td>5-10</td>
<td>5-10</td>
<td>5-10</td>
</tr>
</tbody>
</table>

### Active Metabolites

- **Clarithromycin:**
  - 14-hydroxyclarithromycin
  - Activity often not accounted for in vitro testing
- **Dirithromycin:**
  - erythromycylamine

### Differences in Intrapulmonary Antimicrobial Disposition

**Single-Dose Studies**

<table>
<thead>
<tr>
<th>Concentration (µg/ml)</th>
<th>Time (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>amoxicillin</td>
<td>1-2</td>
</tr>
<tr>
<td>cefuroxime</td>
<td>4-6</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>6</td>
</tr>
<tr>
<td>ciprofloxacin</td>
<td>6</td>
</tr>
</tbody>
</table>

Wise et al., Conte et al., various sources
Macrolides and Related Antibiotics
John A. Bosso, Pharm.D.

**Macrolide Intrapulmonary Distribution**

![Graph showing intrapulmonary distribution of macrolides](image)

- **Plasma**
- **ELF**

**Macrolide Pharmacodynamics**

- **Erythromycin**
  - Time-dependent (%T>MIC)
- **Clarithromycin & Azilides**
  - Time- and concentration-dependent (AUC/MIC)

**Major Macrolide Drug Interactions**

Mediated through inhibition of CYP3A4
- Astemizole
- Carbamazepine
- Cyclosporin
- Disopyramide
- Midazolam
- Quinidine

Mediated through enzyme induction
- Terfenadine
- Theophylline
- Triazolam
- Zidovudine

**Major Macrolide Drug Interactions**

- Rifampin
- Rifabutin
Macrolides and Related Antibiotics
John A. Bosso, Pharm.D.

Macrolide Drug Interactions
• Mostly likely with erythromycin
• Much less likely with clarithromycin and dirithromycin
• Rare if any with azithromycin

Macrolide Side Effects
• General
  – Gastrointestinal (30% with erythromycin)
  – Ototoxicity
    • Dose-related; usually reversible
    • Auditory or vestibular
  – Hepatotoxicity (rare)
  – QTc prolongation
• Specific
  – Taste perversion with clarithromycin and erythromycin
  – Phlebitis (4%) with IV form of erythromycin

Torsades de pointes
• A polymorphic ventricular tachycardia related to prolongation of the QT interval
• Risk factors for occurrence with macrolides:
  – Patients with electrolyte disturbances
  – Elderly females
  – Concomitant diseases (e.g., cardiac)
  – Concomitant drugs
    • Certain antiarrhymics and others that prolong the QT interval

Shaffer et al. CID 2002;35:197-200.

Indications for Macrolides

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>Erythromycin</th>
<th>Clarithromycin</th>
<th>Azithromycin</th>
<th>Dirithromycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval in pediatrics?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>±</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Otitis</td>
<td>±</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lower respiratory tract infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+*</td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. pyogenes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. trachomatis</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L. pneumophila</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. pneumoniae</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| *does not include H. influenzae

PHRMP732.macrlld.bosso.rev 7.06
Indications for Macrolides

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>Erythromycin</th>
<th>Clarithromycin</th>
<th>Azithromycin</th>
<th>Dirithromycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexually transmitted diseases</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Lymphogranuloma venereum</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Chancroid</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Syphilis</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- NGU</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncomplicated skin &amp; skin structure</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>- Diphtheria</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Acne vulgaris</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Disseminated MAC</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>- Helicobacter pylori (ulcer)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

Misc. Issues

- Controversy regarding role in empiric therapy of respiratory tract infections due to apparent *S. pneumoniae* resistance
- Non-antibacterial effects
  - Anti-inflammatory
  - Mucolytic
  - Ciliary effects
  - Immunomodulatory

Macrolide Immunopharmacologic Effects

*Effects upon bacterial virulence*

- Clarithromycin reduces production of:
  - DNAase
  - protease
  - Endotoxin A
  - Exoenzymes

- Clarithromycin reduces:
  - the potential for adhesion
  - reduces motility
  - alters cellular morphology
  - reduces activity of beta haemolysin

Macrolides / Azalides

**Advantages**

- Good activity against:
  - typical* and
  - atypical pathogens
- Can be used in penicillin-allergic patients
- Generally safe and well tolerated

**Disadvantages**

- No activity against erythromycin-resistant *S. pneumoniae*
- Penicillin resistance in *S. pneumoniae* is often associated with cross-resistance to macrolides
- Tissue accumulation with azithromycin
- Multiple-daily dosing with most macrolides
- Once-daily dosing not supported by pharmacokinetics

*Erythromycin and clarithromycin have relatively low activity against *H. influenzae.*
**Experimental**

Roxithromycin  
- (Phase III)

**KETOLIDES**

- Macrolide-like compounds  
- Inhibitors of protein synthesis  
- Spectrum  
  - *H. influenzae*, *M. catarrhalis*, *C. pneumoniae*, *M. pneumoniae*, macrolide-resistant Gram-positives  
  - Less active vs. *L. pneumophila*  
- Telithromycin and ABT-773

---

**CHEMICAL STRUCTURE**


---

**TELITHROMYCIN IN VITRO ACTIVITY AGAINST TYPICAL PATHOGENS**

<table>
<thead>
<tr>
<th>Organism (N)</th>
<th>MIC (µg/mL)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S pneumoniae</em> (16,672)</td>
<td>0.015</td>
<td>0.5</td>
</tr>
<tr>
<td><em>H influenzae</em> (8064)</td>
<td>1.0</td>
<td>2.0</td>
</tr>
<tr>
<td>(β-lactamase positive; 1631)</td>
<td>2.0</td>
<td>4.0</td>
</tr>
<tr>
<td><em>M catarrhalis</em> (1156)</td>
<td>0.06</td>
<td>0.12</td>
</tr>
<tr>
<td>(β-lactamase positive; 1071)</td>
<td>0.06</td>
<td>0.12</td>
</tr>
<tr>
<td><em>S aureus</em> (methicillin-susceptible; 1775)</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td><em>S pyogenes</em> (3918)</td>
<td>0.03</td>
<td>0.03</td>
</tr>
</tbody>
</table>

TELITHROMYCIN IN VITRO ACTIVITY AGAINST ATYPICAL PATHOGENS

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>MIC (µg/mL)</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt;</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>M pneumoniae</td>
<td></td>
<td>0.008</td>
<td>0.008</td>
<td>0.008–0.06</td>
</tr>
<tr>
<td>(N=47)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C pneumoniae</td>
<td></td>
<td>0.0625</td>
<td>0.25</td>
<td>0.031–2</td>
</tr>
<tr>
<td>(N=19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L pneumophila</td>
<td>f&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.008</td>
<td>0.015</td>
<td>&lt;0.004–0.015</td>
</tr>
<tr>
<td>(N=26)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


TELITHROMYCIN IN VITRO ACTIVITY AGAINST ANTIBIOTIC-RESISTANT S. PNEUMONIAE<sup>1</sup>

<table>
<thead>
<tr>
<th>Resistance Phenotype (N)</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt;</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrolide-susceptible (11,384)</td>
<td>0.015</td>
<td>0.015</td>
<td>0.002–1</td>
</tr>
<tr>
<td>Macrolide-resistant (5,288)</td>
<td>0.12</td>
<td>1.0</td>
<td>0.008–8</td>
</tr>
<tr>
<td>erm&lt;sub&gt;B&lt;/sub&gt; (657)</td>
<td>0.06</td>
<td>0.5</td>
<td>0.008–8</td>
</tr>
<tr>
<td>mef&lt;sub&gt;A&lt;/sub&gt; (436)</td>
<td>0.12</td>
<td>0.5</td>
<td>0.008–1</td>
</tr>
<tr>
<td>mef&lt;sub&gt;A&lt;/sub&gt; + erm&lt;sub&gt;B&lt;/sub&gt; (71)</td>
<td>0.5</td>
<td>0.5</td>
<td>0.06–1</td>
</tr>
<tr>
<td>Penicillin-resistant (4,027)</td>
<td>0.12</td>
<td>1.0</td>
<td>0.004–8</td>
</tr>
<tr>
<td>Levofloxacin-resistant (154)</td>
<td>0.03</td>
<td>0.5</td>
<td>0.004–1</td>
</tr>
<tr>
<td>Multi-drug resistant (1,500)*</td>
<td>0.12</td>
<td>1.0</td>
<td>0.008–8</td>
</tr>
</tbody>
</table>

*Resistant to penicillin, the macrolides, TMP/SXT, and tetracycline

Data on file (PROTEKT Studies) [N=16,672]. Aventis Pharmaceuticals. Bridgewater, NJ.

IN VITRO ACTIVITY AGAINST MACROLIDE-RESISTANT S. PNEUMONIAE

Susceptibility of Resistant S pneumoniae to Telithromycin<sup>1</sup>

![Graph showing susceptibility](image)


IN VITRO ACTIVITY AGAINST H. INFLUENZAE

Susceptibility of H. influenzae

![Graph showing susceptibility](image)


2. KETEK<sup>®</sup> (telithromycin) Prescribing Information. Aventis Pharmaceuticals. Bridgewater, NJ.
TELITHROMYCIN
PHARMACOKINETIC OVERVIEW

Mean Pharmacokinetics of QD 800-mg Doses in 18 Healthy Adults

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Single dose</th>
<th>Multiple dose (7 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{max} (μg/mL)</td>
<td>1.9</td>
<td>2.27</td>
</tr>
<tr>
<td>T_{max} (h)*</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>AUC_{0-24} (μg*h/mL)</td>
<td>8.25</td>
<td>12.5</td>
</tr>
<tr>
<td>Terminal T_{1/2} (h)</td>
<td>7.16</td>
<td>9.81</td>
</tr>
<tr>
<td>C_{min} (μg/mL)</td>
<td>0.03</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*Median values.

- 57% absolute bioavailability
- Absorption not affected by food
- Total in vitro protein binding is approximately 60% to 70% and is primarily due to human serum albumin
- Metabolism accounts for approximately 70% of the dose
- Elimination is by multiple pathways: 7% by biliary and/or intestinal secretion; 13% unchanged by renal excretion; and 37% by the liver

FDA-APPROVED RESPIRATORY INDICATIONS

- Acute Bacterial Sinusitis
  - S pneumoniae
  - H influenzae
  - M catarrhalis
  - S aureus
- Acute Bacterial Exacerbation of Chronic Bronchitis
  - S pneumoniae
  - H influenzae
  - M catarrhalis
- Community-Acquired Pneumonia of Mild to Moderate Severity
  - S pneumoniae
  - S pneumoniae (multi-drug resistant)
  - H influenzae
  - M catarrhalis
  - C pneumoniae
  - M pneumoniae
- No Enteric Gram-Negative Coverage

ADVERSE EVENT PROFILE SIMILAR TO COMPARATORS

All Treatment-emergent Adverse Events Reported in Phase III Controlled Clinical Trials

<table>
<thead>
<tr>
<th>Adverse Event*</th>
<th>Telithromycin n=2702</th>
<th>Comparators\† n=2139</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>10.8%</td>
<td>8.6%</td>
</tr>
<tr>
<td>Nausea</td>
<td>7.9%</td>
<td>4.6%</td>
</tr>
<tr>
<td>Headache</td>
<td>5.5%</td>
<td>5.8%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3.7%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.9%</td>
<td>2.2%</td>
</tr>
<tr>
<td>Loose Stool</td>
<td>2.3%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>1.6%</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

*Based on the frequency of possibly related adverse events >2% in KETEK or comparator groups.
†Includes the comparators from all combined Phase III studies: amoxicillin, amoxicillin/clavulanate, cefuroxime, clarithromycin, trovafloxacin.

Dosing and Drug Interaction Issues

- Chiefly removed via metabolism (CYP 3A4)
- No dosing adjustment needed in hepatic impairment or elderly
- Proper dosing with severe renal dysfunction unknown
- CYP-drug interactions!
  - Discontinue simvastatin, lovastatin and atorvastatin during telithromycin therapy
Telithromycin and Hepatotoxicity

- In June of 2006 the FDA required a change in the PI regarding the potential for serious hepatic toxicity based on several case reports

http://www.fda.gov/bbs/topics/NEWS/2006/NEW01401.html

Case:

FZX, a 41 year old white female, is seen in the outpatient department for complaints of low grade fever, cough, and mild respiratory distress. CXR shows light, patchy infiltrates. The attending physician suspects mycoplasma pneumonia and wishes to treat the patient with erythromycin. However, before writing a prescription, she seeks your advice. She explains that she has heard a lot lately from the pharmaceutical company representatives about the “new erythromycins” and asks for your appraisal and advice in selecting appropriate macrolide therapy for this patient.

Questions to Address:

1. What are the differences between the three major macrolides (erythromycin, clarithromycin and azithromycin) in terms of spectrum of antibacterial activity?

2. Are there important pharmacokinetic properties which distinguish one macrolide from another? If so, what are they?

3. Are there important differences in side effect profiles that help distinguish between the various macrolides?

4. Are there important drug interactions to avoid with erythromycin? Do these interactions, or others, occur with the other macrolides?

5. Based upon the above discussion, are there differences in clinical indications of the various macrolides of which the pharmacist should be aware?