



## Therapeutic Class Review<sup>SM</sup>

### Anti-infectives - azithromycin (Zmax<sup>TM</sup>)

November 2005

**New Product for Review:**

azithromycin (Zmax<sup>TM</sup>) [Pfizer]

**Dossier Provided by Manufacturer: Yes**

**Dossier Evaluation: 2**

- 1 - dossier w/missing components
- 2 - all components, except pharmacoeconomic model
- 3 - all components, well done

**Issues:**

- Is there sufficient evidence to demonstrate the efficacy of a single dose of azithromycin (Zmax) in the treatment of community-acquired pneumonia (CAP) and acute bacterial sinusitis (ABS)?
- Is there evidence that Zmax is superior to our current preferred/formulary products with regard to efficacy in the treatment of CAP and ABS?
- Is there evidence that Zmax is better tolerated than our current preferred/formulary products?
- Is there evidence that the perfect adherence inherent in the single dose Zmax regimen improves outcomes and decreases the emergence of antibiotic resistance?

**Executive Summary**

- Zmax is a new formulation of azithromycin that offers the convenience of a single-dose treatment for CAP and ABS.
- Zmax will be strongly marketed by the manufacturer and is expected to be a patent replacement for Zithromax. (Zithromax is no longer patent protected).
- Zithromax is approved as a single-dose treatment for certain sexually transmitted diseases, however the manufacturer has not pursued its use in other indications such as CAP or ABS.

**Evidence:**

- There is currently no published evidence that supports the efficacy of Zmax in the treatment of CAP or ABS.
  - There are two unpublished trials of uncertain validity that conclude that Zmax is similar to a standard treatment course of Biaxin XL or Levaquin in the treatment of CAP.

- There is one unpublished trial of uncertain validity that concludes that Zmax is similar to a standard treatment course of Levaquin in the treatment of ABS.
- There is no evidence that Zmax has superior efficacy over preferred/formulary agents in the treatment of CAP or ABS (including Zithromax 3- and 5-day regimens).
- There is no evidence that Zmax has improved safety or is better tolerated than the preferred/formulary agents used for the treatment of CAP or ABS (including Zithromax 3- and 5-day regimens).
- There is no evidence that Zmax has improved tolerability over a single 2 gram dose of Zithromax tablets.
- The single-dose Zmax regimen has not been shown to improve outcomes or decrease the emergence of antibiotic resistance relative to other antibiotic regimens.

### **Decision**

- Maintain non-preferred/non-formulary status for azithromycin extended-release oral suspension (Zmax) there is no evidence that it has improved efficacy, tolerability, or safety over preferred/formulary alternatives.

## I. Products

Drug Product	Date of FDA Approval	FDA approved for:			Dose: adult (oral)	Potential Off-Label Uses
		CAP	ABS	ABEC		
<b>Beta-lactams</b>						
amoxicillin <sup>1</sup> (generics)	1970's		X		ABS: 500 mg t.i.d. x 10-14 days Respiratory tract infections: 500 mg q8h x 10 days, up to 1 Gm q6h x 10 days	
amoxicillin/clavulanate (Augmentin <sup>®</sup> ) <sup>2</sup>	8/1984		X		ABS: 500 mg q8h x 10 days, or 875 mg q12h x 10 days  Lower respiratory infections: 500 mg q8h x 10 days, or 875 mg q12h x 10 days	
amoxicillin/clavulanate [1000 mg/62.5 mg/tablet] (Augmentin <sup>®</sup> XR) <sup>3</sup>	9/2002	X	X		CAP: 2 tabs q12h x 7-10 days ABS: 2 tabs q12h x 10 days	
cefepodoxime (Vantin <sup>®</sup> ) <sup>4</sup>	8/1992	X	X	X	CAP: 200 mg q12h x 10 days ABS: same ABEC: same	
cefuroxime axetil (Ceftin <sup>®</sup> ) <sup>5</sup>	12/1987		X	X	ABS: 250 mg b.i.d. x 10 days ABEC: 250-500mg b.i.d. x 10days	
cefdinir (Omnicef <sup>®</sup> ) <sup>6</sup>	12/1997	X	X	X	CAP: 300 mg q.12h x 10 days ABS: 300 mg q 12h x 10 days; or 600 mg q.d. x 10 days ABEC: 300 mg q 12h for 10 days; or 600 mg q.d. x 5-10 days	
<b>Macrolides</b>						
azithromycin (Zithromax <sup>®</sup> ) <sup>1,7</sup>	7/1996	X	X	X	CAP: 500 mg day 1 250 mg q.d. days 2-5 ABS: 500 mg q.d x 3 days ABEC: 500 mg q.d. x 3 days; or 500 mg day 1, 250mg q.d. days 2-5.	traveler's diarrhea, etc
azithromycin (Zmax <sup>®</sup> ) <sup>1,8</sup>	6/2005	X	X		CAP: 2 Gm x 1 dose ABS: 2 Gm x 1 dose	ABEC
clarithromycin (Biaxin <sup>®</sup> ) <sup>9</sup>	10/1991	X	X	X	CAP: 250 mg q12h x 7-14 days ABS: 500 mg q12h x 14 days ABEC: 250-500 mg q12h x 7-14 days	
clarithromycin (Biaxin <sup>®</sup> XL) <sup>9</sup>	3/2000	X	X	X	CAP: 1000 mg q.d. x 7 days ABS: 1000 mg q.d. x 14 days ABEC: 1000 mg q.d. x 7 days	
erythromycin <sup>1</sup> (generic)	1950's				Respiratory tract infections: 250 mg q.i.d.; or 500 mg b.i.d. x 10 days	gastroparesis, etc.
telithromycin (Ketek <sup>®</sup> ) <sup>1,10</sup>	4/2004	X	X	X	CAP: 800 mg q.d. for 7-10 days ABS: 800 mg q.d. for 5 days ABEC: 800 mg q.d. for 5 days	pharyngitis/ tonsillitis

## I. Products (continued)

Drug Product	Date of FDA Approval	FDA approved for:			Dose: adult (oral)	Potential Off-Label Uses
		CAP	ABS	ABEC		
<b>Fluoroquinolones</b>						
gatifloxacin (Tequin®) <sup>11</sup>	12/1999	X	X	X	CAP: 400 mg q.d. for 7-14 days ABS: 400 mg q.d. for 10 days ABEC: 400 mg q.d. for 5 days	
gemifloxacin (Factive®) <sup>1, 12</sup>	4/2003	X		X	CAP: 320 mg q.d. for 7 days ABEC: 320 mg q.d. for 5 days	ABS
levofloxacin (Levaquin®) <sup>1, 13</sup>	12/1996	X	X	X	CAP: 500 mg q.d. for 7-14 days; or 750 mg q.d. for 5 days ABS: 500 mg q.d. for 10-14 days; or 750 mg q.d. for 5 days ABEC: 500 mg q.d. for 7 days	STDs, infectious diarrhea
moxifloxacin (Avelox®) <sup>14</sup>	4/2001	X	X	X	CAP: 400 mg q.d. for 7-14 days ABS: 400 mg q.d. for 10 days ABEC: 400 mg q.d. for 5 days	
<b>Miscellaneous</b>						
doxycycline (Vibramycin®) <sup>15</sup>	12/1967				Respiratory tract infections: 100 mg q12h for 10 days	

**I. Products (continued)**

**Table 2: FDA approved indications with approved microorganisms covered by antibiotic:**

	Antibiotic	CAP	ABS	ACEB
Beta-lactams	amoxicillin <sup>1</sup>	Respiratory tract infections caused by the following organisms: <i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i>		
	Augmentin <sup>2</sup>	<i>Staphylococcus aureus</i> <i>Streptococcus pneumoniae</i> beta-lactamase producing strains of: <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Moraxella catarrhalis</i> <i>Klebsiella pneumoniae</i>	<i>Staphylococcus aureus</i> <i>Streptococcus pneumoniae</i> beta-lactamase producing strains of: <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Moraxella catarrhalis</i> <i>Klebsiella pneumoniae</i>	
	Vantin <sup>4</sup>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>
	Ceftin <sup>5</sup>		<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i>
	Omnicef <sup>6</sup>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Moraxella catarrhalis</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Moraxella catarrhalis</i>
Macrolide antibiotics	Biaxin <sup>9</sup>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Chlamydia pneumoniae</i> <i>Mycoplasma pneumoniae</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Moraxella catarrhalis</i>
	erythromycin <sup>1</sup>	Respiratory tract infections caused by the following organisms: <i>Streptococcus pneumoniae</i> <i>Streptococcus pyogenes</i> <i>Mycoplasma pneumoniae</i> <i>Legionella pneumophila</i>		
	Ketek <sup>10</sup>	<i>Streptococcus pneumoniae</i> (including MDRSP) <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i> <i>Chlamydia pneumoniae</i> <i>Mycoplasma pneumoniae</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i> <i>Staphylococcus aureus</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>
	Zithromax <sup>7</sup>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Chlamydia pneumoniae</i> <i>Mycoplasma pneumoniae</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>
	Zmax <sup>8</sup>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Chlamydia pneumoniae</i> <i>Mycoplasma pneumoniae</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>	

**I. Products (continued)**

**Table 2: FDA approved indications along with microorganisms covered by specific antibiotics:**

Fluoroquinolone	Avelox <sup>14</sup>	<i>Streptococcus pneumoniae</i> (including MDRSP) <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i> <i>Staphylococcus aureus</i> <i>Klebsiella pneumoniae</i> <i>Mycoplasma pneumoniae</i> <i>Chlamydia pneumoniae</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Klebsiella pneumoniae</i> <i>Staphylococcus aureus</i> <i>Moraxella catarrhalis</i>
	Factive <sup>12</sup>	<i>Streptococcus pneumoniae</i> (including MDRSP) <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i> <i>Klebsiella pneumoniae</i> <i>Mycoplasma pneumoniae</i> <i>Chlamydia pneumoniae</i>		<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Moraxella catarrhalis</i>
	Levaquin <sup>13</sup>	<i>Staphylococcus aureus</i> <i>Streptococcus pneumoniae</i> (including MDRSP) <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Klebsiella pneumoniae</i> <i>Moraxella catarrhalis</i> <i>Chlamydia pneumoniae</i> <i>Legionella pneumophila</i> <i>Mycoplasma pneumoniae</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>	<i>Staphylococcus aureus</i> <i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Moraxella catarrhalis</i>
	Tequin <sup>11</sup>	<i>Streptococcus pneumoniae</i> (including MDRSP) <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Moraxella catarrhalis</i> <i>Staphylococcus aureus</i> <i>Mycoplasma pneumoniae</i> <i>Chlamydia pneumoniae</i> <i>Legionella pneumophila</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i> <i>Moraxella catarrhalis</i> <i>Staphylococcus aureus</i>
Miscellaneous	doxycycline <sup>15</sup>	Respiratory tract infections caused by the following organisms: <i>Mycoplasma pneumoniae</i> <i>Haemophilus influenzae</i> <i>Klebsiella sp.</i> <i>Streptococcus pneumoniae</i> <i>Bacillus anthracis</i>		

MDRSP = multi-drug resistant *S. pneumoniae*

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