



Therapeutic Class ReviewSM

azithromycin (ZmaxTM)

November 2005

New Product for Review:
azithromycin (ZmaxTM) [Pfizer]

Dossier Provided by Manufacturer: Yes

Available Therapeutic Alternatives:

Product [manufacturer]	Formulary Status	Community-acquired pneumonia (CAP)	Acute bacterial sinusitis (ABS)
Beta-lactams:			
amoxicillin [generics]	F	X*	X
amoxicillin/clavulanic acid (Augmentin [®]) [generic]	F	X*	X
amoxicillin/clavulanic acid (Augmentin XR [®]) [GlaxoSmithKline]	NF	X	X
cefdinir (Omnicef [®]) [Abbott Laboratories]	NF	X	X
cefepodoxime (Vantin [®]) [generic]	NF	X	X
cefuroxime axetil (Ceftin [®]) [generic]	F	X*	X
Macrolides:			
azithromycin (Zithromax [®]) [Pfizer]	F	X	X
clarithromycin (Biaxin [®]) [generic]	F	X	X
clarithromycin ext. release (Biaxin [®] XL) [Abbott]	NF	X	X
erythromycin [generic]	F	X	X
telithromycin (Ketek [®]) [Aventis]	NF	X	X
Fluoroquinolones:			
gatifloxacin (Tequin [®]) [Bristol-Myers Squibb]	NF	X	X
gemifloxacin (Factive [®]) [Oscient]	NF	X	
levofloxacin (Levaquin [®]) [Ortho-McNeil]	NF	X	X
moxifloxacin (Avelox TM)	F	X	X
Miscellaneous:			
doxycycline (Vibramycin [®]) [generic]	F	X*	X*

F = formulary/preferred medication
NF = non-formulary/non-preferred medication
indication

X = FDA approved indication
X* = not FDA approved, but an established treatment for given indication

Executive Summary

- Zmax is a new formulation of azithromycin that offers the convenience of a single-dose treatment for CAP and ABS.
- Zmax will 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 as a single-dose treatment 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 - There are two unpublished trials of uncertain validity that conclude that Zmax is similar to a standard treatment course of Biaxin XL or Levaquin in the treatment of CAP.
 - There is one unpublished trial of uncertain validity that concludes that Zmax is similar to a standard treatment course of Levaquin in the treatment of ABS.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 Gm 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.

Conclusion

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

Products

Drug Product	Date of FDA Approval	FDA approved for:			Dose: adult (oral)	AWP or MAC Cost*	Potential Off-Label Uses
		CAP	ABS	ABEC			
Beta-lactams							
amoxicillin ¹ (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	\$3 \$ 3 to \$4	
amoxicillin/clavulanate (Augmentin [®]) ²	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	\$80 \$80 \$80 \$80	
amoxicillin/clavulanate [1000 mg/62.5 mg/tablet] (Augmentin [®] XR) ³	9/2002	X	X		CAP: 2 tabs q12h x 7-10 days ABS: 2 tabs q12h x 10 days	\$102 to \$146 \$146	
cefepodoxime (Vantin [®]) ⁴	8/1992	X	X	X	CAP: 200 mg q12h x 10 days ABS: same ABEC: same	\$87 \$87 \$87	
cefuroxime axetil (Ceftin [®]) ⁵	12/1987		X	X	ABS: 250 mg b.i.d. x 10 days ABEC: 250-500mg b.i.d. x 10days	\$27 \$27 to \$50	
cefdinir (Omnicef [®]) ⁶	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	\$99 \$99 \$99 \$99 \$50 to \$99	
Macrolides							
azithromycin (Zithromax [®]) ^{1,7}	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.	\$52 \$52 \$52	traveler's diarrhea, etc
azithromycin (Zmax [®]) ^{1,8}	6/2005	X	X		CAP: 2 Gm x 1 dose ABS: 2 Gm x 1 dose	\$52	ABEC
clarithromycin (Biaxin [®]) ⁹	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	\$50 to \$100 \$100 \$100	
clarithromycin (Biaxin [®] XL) ⁹	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	\$78 \$157 \$78	
erythromycin ¹ (generic)	1950's				Respiratory tract infections: 250 mg q.i.d.; or 500 mg b.i.d. x 10 days	\$6	gastroparesis, etc.
telithromycin (Ketek [®]) ^{1,10}	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	\$81 to \$116 \$58 \$58	pharyngitis/ tonsillitis

Products (continued)

Drug Product	Date of FDA Approval	FDA approved for:			Dose: adult (oral)	AWP or MAC Cost*	Potential Off-Label Uses
		CAP	ABS	ABEC			
Fluoroquinolones							
gatifloxacin (Tequin [®]) ¹¹	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	\$72 to \$144 \$103 \$52	
gemifloxacin (Factive [®]) ^{1, 12}	4/2003	X		X	CAP: 320 mg q.d. for 7 days ABEC: 320 mg q.d. for 5 days	\$144 \$103	ABS
levofloxacin (Levaquin [®]) ^{1, 13}	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	\$83 to \$165 \$110 \$118 to \$165 \$110 \$83	STDs, infectious diarrhea
moxifloxacin (Avelox [®]) ¹⁴	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	\$78 to \$156 \$112 \$56	
Miscellaneous							
doxycycline (Vibramycin [®]) ¹⁵	12/1967				Respiratory tract infections: 100 mg q12h for 10 days	\$2 to \$3	

*AWP (average wholesale price) based on First Data Bank or MAC (maximum allowable cost) as of August 2005 for 1 course of therapy.

Products (continued)

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

Antibiotic		CAP	ABS	ACEB
Beta-lactams	amoxicillin ¹	Respiratory tract infections caused by the following organisms: <i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i>		
	Augmentin ²	<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 ⁴	<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 ⁵		<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i>	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Haemophilus para influenzae</i>
	Omnicef ⁶	<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 ⁹	<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 ¹	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 ¹⁰	<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 ⁷	<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 ⁸	<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>	

Products (continued)

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

Fluoroquinolone	Avelox ¹⁴	<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 ¹²	<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 ¹³	<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 ¹¹	<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 ¹⁵	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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