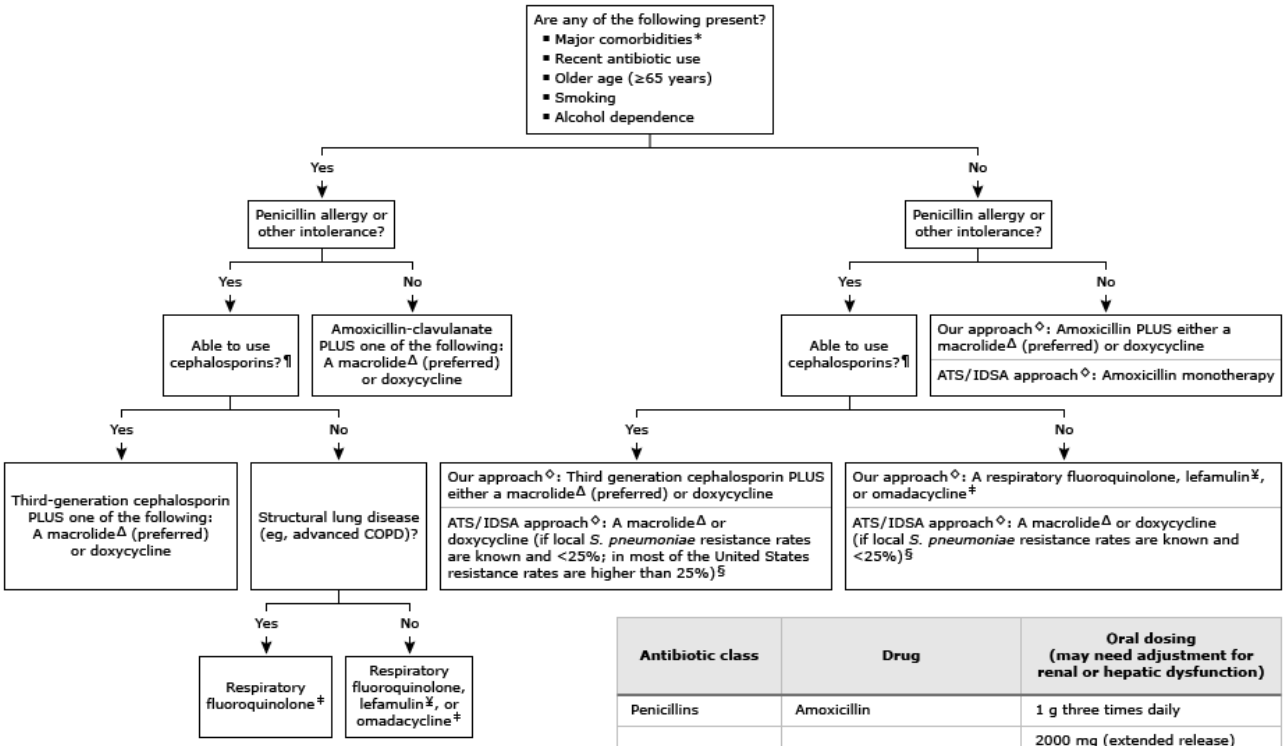
Community-acquired pneumonia: Empiric outpatient antibiotic selection in adults



Antibiotic class	Drug	Oral dosing (may need adjustment for renal or hepatic dysfunction)
Penicillins	Amoxicillin	1 g three times daily
Extended-spectrum beta-lactams	Amoxicillin-clavulanate	2000 mg (extended release) twice daily
		875 mg orally twice daily
	Cefpodoxime (3rd generation)	200 mg twice daily
	Cefditoren (3rd generation)	400 mg twice daily
Macrolides	Azithromycin	500 mg on first day then 250 mg daily
	Clarithromycin	500 mg twice daily or 1g (extended release) once daily
Tetracyclines	Doxycycline	100 mg twice daily
	Omadacycline	300 mg twice daily on day 1, then 300 mg once daily
Respiratory fluoroquinolones	Levofloxacin	750 mg once daily
	Moxifloxacin	400 mg once daily
	Gemifloxacin	320 mg once daily
Pleuromutilin	Lefamulin	600 mg twice daily
A 5-day course is sufficient for most outpatients. In general, a follow-up visit or communication is indicated within a few days of starting treatment to ensure that the patient is afebrile and improving.		

For all patients, our empiric regimens are designed to target:◇

- *Streptococcus pneumoniae* (most common bacterial CAP pathogen)
- Atypical pathogens (eg, *Legionella* spp, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*)

Coverage is expanded in those with comorbidities, older age, or recent antibiotic use to include or better treat:

- Beta-lactamase-producing *Haemophilus influenzae*
- *Moraxella catarrhalis*
- Methicillin-susceptible *Staphylococcus aureus*

For patients with structural lung disease (eg, advanced COPD), coverage is further expanded to include Enterobacteriaceae, such as *Escherichia coli* and *Klebsiella* spp.

ATS/IDSA: American Thoracic Society/Infectious Diseases Society of America; COPD: chronic obstructive pulmonary disease; CAP: community-acquired pneumonia; IgE: immunoglobulin E.

* Major comorbidities include but are not limited to chronic heart, renal, or liver disease, diabetes mellitus, asplenia, and immunosuppression.

¶ Patients with mild non-IgE-mediated reactions (eg, maculopapular rash) to penicillin or known cephalosporin tolerance can generally use later-generation cephalosporins safely. Patients with IgE-mediated reactions (hives, angioedema, anaphylaxis) or severe delayed reactions should generally use other agents. Refer to the UpToDate text on penicillin hypersensitivity reactions for detail.

Δ Reasons to avoid macrolides include baseline prolonged QTc interval or risk for QTc prolongation (eg, hypokalemia, hypomagnesemia, clinically significant bradycardia, or use of other QT-prolonging agents).

◇ Our approach differs from the ATS/IDSA, which recommend monotherapy with amoxicillin, doxycycline, or a macrolide (in areas where macrolide resistance is low) as options for patients without comorbidities or risk factors for drug-resistant *S. pneumoniae*. By contrast, we prefer to treat all patients with a regimen that treats most strains of drug-resistant *S. pneumoniae* and atypical pathogens for all patients because the potential to reduce morbidity is high and the downside of a short course of therapy for most patients is low. Refer to the UpToDate text for detail.

§ For macrolides, resistance rates among *S. pneumoniae* are often >30% in the United States and typically >25% for most parts of the world, apart from some regions in Northern Europe. For doxycycline, resistance rates are less well established but are approximately 10 to 20% in the United States and likely rising.

¥ Lefamulin is a newer agent that is active against most CAP pathogens including *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, *S. aureus*, and atypical pathogens. Although lefamulin lacks activity against Enterobacteriaceae (eg, *Klebsiella* spp and *E. coli*) and thus is not appropriate for patients with structural lung disease, its more targeted spectrum makes it less disruptive to the microbiome. Clinical experience with lefamulin is limited, and it is not recommended in moderate to severe hepatic dysfunction, pregnancy, breastfeeding, known long QT syndrome, or with concomitant QT-prolonging agents. There are drug interactions with CYP3A4 and P-gp inducers and substrates; in addition, lefamulin tablets are contraindicated with QT-prolonging CYP3A4 substrates. Refer to the Lexicomp drug monograph and UpToDate text for detail.

‡ Omadacycline is another newer agent that is active against most CAP pathogens, including Enterobacteriaceae. It is a potential alternative for patients who cannot tolerate beta-lactams (or other agents) and want to avoid fluoroquinolones.

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