





EMLc

ATC codes: J01CA04

Indication	Acute pharyngitis <span>ICD11 code: CA02</span>
INN	Amoxicillin
Medicine type	Chemical agent
Antibiotic groups	 ACCESS
List type	Core
Formulations	Oral > Liquid: 125 mg per 5 mL (as trihydrate) powder for oral liquid ; 250 mg per 5 mL (as trihydrate) powder for oral liquid (EMLc) Oral > Solid: 250 mg (as trihydrate) ; 500 mg (as trihydrate) Parenteral > General injections > unspecified: 250 mg in vial (as sodium) powder for injection ; 500 mg in vial (as sodium) powder for injection ; 1 g in vial (as sodium) powder for injection
EML status history	First added in 2017 (TRS 1006)
Sex	All
Age	Also recommended for children
Therapeutic equivalence	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more <a href="#">about patents</a> . 
Wikipedia	<a href="#">Amoxicillin</a> 
DrugBank	<a href="#">Amoxicillin</a> 

### Expert Committee recommendation

The Expert Committee noted that the appropriate first-line treatment option for pharyngitis is watchful waiting, symptom relief and no antibiotic treatment. For suspected or proved bacterial pharyngitis, the Committee endorsed the use of phenoxymethylpenicillin or amoxicillin as first-choice therapy and clarithromycin (EML) or cefalexin (EML/EMLc) as second-choice therapy. The Committee recommended the addition of clarithromycin to the EMLc (with erythromycin as an alternative) as second-choice therapy for suspected or proven bacterial pharyngitis in children.

### Background

More than 85% of pharyngitis is viral in origin. Pharyngitis is distinct from laryngitis, or inflammation of the larynx, for which there was no evidence for antibiotic effectiveness when objective outcomes were assessed (1). The major cause of bacterial pharyngitis is Group A Streptococcus (GAS). It is notable that penicillin resistance has yet to be demonstrated by these bacteria, although resistance to macrolides has increased. The major reason for treating GAS, other than symptomatic relief, has been to reduce complications such as rheumatic fever and post-streptococcal glomerulonephritis.

### Summary of evidence

A 2013 Cochrane review of antibiotic therapy for GAS pharyngitis in 17 randomized controlled trials (RCTs; 5352 participants) found no difference in symptom resolution between cephalosporins and penicillin (odds ratio (OR) 0.79; 95% confidence interval (CI) 0.55–1.12) but lower clinical relapse in adults given cephalosporins (OR 0.55; 95% CI 0.31–0.99) and no difference between

macrolides and penicillin (OR 1.11; 95% CI 0.92–1.35) (2). Duration of treatment has also been studied, with the premise that a shorter duration of antibiotic therapy, if effective, can reduce development of resistance, adverse events and cost. A 2012 Cochrane review summarized evidence for short-duration treatment (2–6 days) with newer agents (including azithromycin and clarithromycin) versus 10 days of penicillin (20 RCTs; 13 102 cases) in children with group A beta haemolytic streptococcus pharyngitis (3). The findings were in favour of shorter duration of treatment, with a reduction in the duration of fever (mean difference (MD) –0.30 days; 95% CI –0.45 to –0.14), throat soreness (MD –0.50 days; 95% CI –0.78 to –0.22), and lower risk of early clinical failure (OR 0.80; 95% CI 0.67–0.94). There were no differences in early bacteriological cure (OR 1.08; 95% CI 0.97–1.20) or late clinical recurrence (OR 0.95; 95% CI 0.83–1.08). However, there was a significantly greater risk of late bacteriological recurrence with the short-duration treatment (OR 1.31; 95% CI 1.16–1.48) (3). Another Cochrane review (27 RCTs; 12 835 participants), which examined complications, reported that antibiotics reduced the risk of developing rheumatic fever (risk ratio (RR) 0.27; 95% CI 0.12–0.60) but there were too few events to comment on glomerulonephritis (4). In terms of suppurative complications, antibiotics reduced the incidence of acute otitis media (RR 0.30; 95% CI 0.15–0.58), acute sinusitis (RR 0.48; 95% CI 0.08–2.76), and peritonsillar abscess within two months (RR 0.15; 95% CI 0.05–0.47) compared with placebo. The RCTs demonstrated the benefit of using antibiotics for GAS pharyngitis to reduce complications, which is of particular relevance in low- and middle-income countries. Although there is evidence that macrolides and cephalosporins may reduce duration of symptoms, this must be weighed against the possibility for resistance to these agents, particularly since penicillin resistance in GAS has never been observed.

## Guidelines

The Infectious Diseases Society of America's Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis was rated as moderate to high quality in the application (5). It recommends penicillin or amoxicillin as the first-line agent for GAS pharyngitis. For individuals with serious penicillin allergy, macrolides (azithromycin or clarithromycin) are recommended.

## Rationale for antibiotic selection

Pharyngitis frequently has a viral cause. Thus, routine practice in some countries is not to treat pharyngitis at all; other countries typically use a delayed antibiotic prescription policy, and yet others heavily rely on microbiological testing to support an indication for antibiotic treatment. In Group A streptococcal infections, antibiotics can reduce the incidence of rheumatic fever and suppurative complications. The fact that the evidence suggests similar overall outcomes with penicillin compared with other antibiotic classes, together with the importance of sparing macrolides and cephalosporins, argues strongly in favour of penicillin or amoxicillin as the first-line antibiotic. Clarithromycin can be used where there is a severe allergy to penicillin. It should be noted that routine skin testing for allergy before first treatment with penicillins, which is current practice in some regions, is not necessary. For patients with known severe allergies who live in regions with high rates of macrolide resistance, cefalexin would be another option.

## Committee considerations

The Expert Committee noted that, since the vast majority of pharyngitis cases are caused by viruses, routine practice in some countries is not to treat the infection with antibiotics, others use a delayed antibiotic prescription policy, and others rely on diagnostic tests to support an indication for antibiotic treatment. Indeed, antibiotics have limited benefit in streptococcal pharyngitis, unless rheumatic fever is still a problem in a particular setting. The Committee also noted the absence of indication for routine skin testing for allergy before first treatment with penicillins. For common community-acquired infections, the main focus has been on empirical treatment choices that are broadly applicable in most countries. Generally, alternatives for use in case of allergy were not considered. The Committee considered the various antibiotics proposed in the application under the guiding principle of parsimony and selected first- and second-choice antibiotics for this indication for inclusion on the EML and/or EMLc. The Committee endorsed the application's proposal. Recommended first- and second-choice antibiotics are reported above. The first-choice antibiotics are those that are generally recommended on the basis of available evidence and are usually narrow-spectrum agents.

## EML recommendations: Acute pharyngitis

### First choice

### Second choice

**WATCHFUL WAITING, SYMPTOM RELIEF AND NO ANTIBIOTIC TREATMENT SHOULD BE CONSIDERED AS THE FIRST-LINE TREATMENT OPTION.**

amoxicillin

cefalexin

phenoxymethylpenicillin

clarithromycin

1. Reveiz L, Cardona AF. Antibiotics for acute laryngitis in adults. Cochrane Database Syst Rev. 2015;(5):CD004783.
2. van Driel ML, De Sutter AI, Keber N, Habraken H, Christiaens T. Different antibiotic treatments for group A streptococcal pharyngitis.
3. Altamimi S, Khalil A, Khalaiwi KA, Milner RA, Pusic MV, Al Othman MA. Short-term late-generation antibiotics versus longer term penicillins for acute tonsillitis.
4. Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. Cochrane Database Syst Rev. 2013;(11):CD000023.
5. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G et al. Clinical practice guideline for the diagnosis and management of acute pharyngitis in children and adolescents.

