


EMLc
ATC codes: [J01CR02](#)

Indication	Acute sinusitis ICD11 code: CA01
INN	Amoxicillin + clavulanic acid
Medicine type	Chemical agent
Antibiotic groups	A ACCESS
List type	Core
Formulations	Parenteral > General injections > IV: 500 mg (as sodium salt) + 100 mg (as potassium salt) powder for injection ; 1000 mg (as sodium salt) + 200 mg (as potassium salt) powder for injection Oral > Liquid: 125 mg + 31.25 mg powder for oral liquid (EMLc) ; 250 mg + 62.5 mg powder for oral liquid (EMLc) Oral > Solid: 500 mg (as trihydrate) + 125 mg (as potassium salt)
EML status history	First added in 2017 (TRS 1006)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents . 
Wikipedia	Amoxicillin + clavulanic acid 
DrugBank	Amoxicillin  , Clavulanic acid (Clavulanate) 

Expert Committee recommendation

The Expert Committee noted that the appropriate first-line treatment option for sinusitis is watchful waiting, symptom relief and no antibiotic treatment. The Committee endorsed the inclusion of amoxicillin and amoxicillin + clavulanic acid for suspected bacterial sinusitis as first-choice treatment on the EML and EMLc.

Background

Sinusitis is generally diagnosed and treated in an ambulatory setting and most clinical trials have been conducted in this setting. Patients are typically treated on a clinical basis with no attempt made to obtain cultures for etiological determination. Given that more than 90% of cases of rhinosinusitis are due to viral infections, many of the trials have been conducted to test whether antibiotics offer any benefit compared with placebo.

Summary of evidence

The question of whether sinusitis actually needs treatment with antibiotics has been addressed in several randomized controlled trials (RCTs). A 2012 Cochrane review (10 RCTs; 2450 participants) compared antibiotics with placebo for adults with rhinosinusitis and found that purulent secretions resolve faster with antibiotics (odds ratio (OR) 1.58; 95% confidence interval (CI) 1.13–2.22) (1). However, 27% of participants given antibiotics, versus 15% of those that received placebo, experienced adverse events (OR 2.10; 95% CI 1.60–2.77). A 2013 Cochrane review of antibiotics for the common cold and purulent rhinitis (11 RCTs;

1047 participants) reported no difference in cure or persistent symptoms (risk ratio (RR) 0.95; 95% CI 0.59–1.51) (2). For adverse effects in the antibiotic group RR was 1.8 (95% CI 1.01–3.21) if antibiotics were initiated in patients with symptoms and signs of sinusitis lasting for 7 days or more. However, a more recent review of six RCTs showed a benefit of antibiotic treatment compared with placebo for symptomatic improvement after 3 days (OR 2.78; 95% CI 1.39–5.58) and 7 days (OR 2.29; 95% CI 1.19–4.41) after initiation in patients with symptoms and signs of sinusitis lasting for 7 days or more (3). After 10 days, however, improvement rates did not differ significantly between patients treated with antibiotics or given placebo (OR 1.36; 95% CI 0.66–2.90). In terms of selection of antibiotics, a 2014 Cochrane review (63 RCTs; 1915 participants) showed that amoxicillin or penicillin was superior to placebo in adults with maxillary sinusitis in terms of clinical failure (RR 0.66; 95% CI 0.47–0.94), but that the risk for clinical failure was higher with cephalosporins or macrolides compared with amoxicillin + clavulanic acid (RR 1.37; 95% CI 1.04–1.80) (4). However, cure or improvement was high in both groups (86% for placebo and 91% in antibiotic group). Adverse events were more common in antibiotic than in placebo groups (median 10.5% difference between groups, range 2–23%). The RCTs demonstrate that antibiotics offer no benefit over placebo for sinusitis related to the common cold, which is most commonly caused by rhinovirus. Amoxicillin or penicillin may offer a moderate clinical benefit to patients with purulent sinusitis but this comes at increased risk of adverse events. Amoxicillin + clavulanic acid was shown to be superior to macrolides or cephalosporins.

Guidelines

The Infectious Diseases Society of America (IDSA) guidelines recommend the use of amoxicillin + clavulanic acid as a first-line agent and a respiratory fluoroquinolone (levofloxacin or moxifloxacin) or doxycycline (for adult patients) in cases of allergy to beta-lactams (5). Amoxicillin + clavulanic acid, as opposed to amoxicillin alone, was recommended because of concern that there is growing prevalence of *Haemophilus influenzae* since the introduction of conjugate pneumococcal vaccines and an increasing prevalence of beta-lactamase production in these strains. However, there are few data to support the exact microbiology following introduction of the 13-valent conjugate pneumococcal vaccine. Other guidelines recommend amoxicillin with or without clavulanic acid and ceftriaxone for children who cannot be treated with oral antibiotics (6, 7). In order to find a positive risk–benefit ratio for treatment decisions, guidelines recommend antibiotics only for patients with no spontaneous resolution within 10 days, severe symptoms, or worsening or double-sickening over 3–4 days.

Rationale for antibiotic selection

Sinusitis frequently does not require antibiotics, particularly when it is associated with the common cold when antibiotics offer limited benefit. Delayed prescribing is another strategy for reducing the use of antibiotics. Evidence from systematic reviews suggests a higher risk of failure with cephalosporins or macrolides compared with amoxicillin + clavulanic acid. Given the principle of using narrower-spectrum agents, amoxicillin alone may be effective; either amoxicillin or amoxicillin + clavulanic acid was therefore proposed as the core choice. Ceftriaxone can be used for severe sinusitis. Fluoroquinolones (levofloxacin, moxifloxacin) should be used only if beta-lactams cannot be used.

Committee considerations

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 Expert 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. Ceftriaxone, levofloxacin and moxifloxacin were excluded. Recommended first-choice antibiotics are reported above. The first-choice antibiotics are those generally recommended on the basis of available evidence and are usually narrow-spectrum agents.

EML recommendations: Acute sinusitis

First choice

Second choice

amoxicillin + clavulanic acid

amoxicillin

1. Lemiengre MB, van Driel ML, Merenstein D, Young J, De Sutter AI. Antibiotics for clinically diagnosed acute rhinosinusitis in adults. *Cochrane Database Syst Rev.* 2012;(10):CD006089.
2. Kenealy T, Arroll B. Antibiotics for the common cold and acute purulent rhinitis. *Cochrane Database Syst Rev.* 2013;(6):CD000247.
3. Burgstaller JM, Steurer J, Holzmann D, Geiges G, Soyka MB. Antibiotic efficacy in patients with a moderate probability of acute rhinosinusitis: a systematic review. *Eur Arch Otorhinolaryngol.* 2016;273(5):1067-77.
4. Ahovuo-Saloranta A, Rautakorpi UM, Borisenko OV, Liira H, Williams JW, Mäkelä M. Antibiotics for acute maxillary sinusitis in adults. *Cochrane Database Syst Rev.* 2014;(2):CD000243.
5. Chow AW, Benninger MS, Brook I, Brozek JL, Goldstein EJ, Hicks LA et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis.* 2012;54(8):e72-112.
6. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, Brook I, Ashok Kumar K, Kramper M et al. Clinical practice guideline (update): adult sinusitis. *Otolaryngol Head Neck Surg.* 2015;152(2 Suppl):S1-39.
7. Wald ER, Applegate KE, Bordley C, Darrow DH, Glode MP, Marcy SM et al. Clinical practice guideline for the diagnosis and management of acute bacterial sinusitis in children aged 1 to 18 years. *Pediatrics.* 2013;132(1):e262-80.

