Benzylpenicillin

Section: 6. Anti-infective medicines > 6.2. Antibacterials > 6.2.1. Access group antibiotics

EMLc | ATC codes: J01CE01

Indication	Bacterial meningitis ICD11 code: 1D01.0Z
INN	Benzylpenicillin
Medicine type	Chemical agent
Antibiotic groups	A ACCESS
List type	Core
Formulations	**Parenteral > General injections > unspecified:** 600 mg in vial powder for injection (=1 million IU as sodium or potassium salt) ; 3 g in vial powder for injection (=5 million IU as sodium or 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	Benzylpenicillin
DrugBank	Benzylpenicillin

Expert Committee recommendation

The Expert Committee endorsed the inclusion on the EML and EMLc of ceftriaxone or cefotaxime as first-choice option for use in suspected acute bacterial meningitis and of chloramphenicol, benzylpenicillin, ampicillin or amoxicillin as second-choice therapy, recognizing that the last three beta-lactams may be added as first-choice options in some countries for suspected acute bacterial meningitis in particular when Listeria is suspected. The Committee recommended the addition of meropenem to the EMLc for use in neonates as a second-choice option to treat suspected acute bacterial meningitis where resistant Gram-negative organisms are the common causative agents.

Background

Acute bacterial meningitis is a medical emergency requiring prompt administration of antibiotics that penetrate well into inflamed meninges. Because of the severity of this infection, evidence from randomized controlled trials (RCTs) is limited; recommendations for antimicrobials are driven largely by susceptibility patterns of the most common pathogens together with experimental work in animal models.

Summary of evidence

In a 2015 systematic review, chloramphenicol was compared with two penicillins, two cephalosporins and one tetracycline (5 RCTs; 1753 patients) (1). Chloramphenicol was associated with higher mortality than the other

antibiotics (risk ratio (RR) 1.27; 95% confidence interval (CI) 1.00–1.60). In contrast, a 2007 Cochrane review (19 RCTs; 1496 patients) that compared third-generation cephalosporins with treatment with penicillin or ampicillin-chloramphenicol found no differences in mortality (risk difference (RD) 0%; 95% CI 3% to 2%), risk of deafness (RD –4%; 95% CI –9% to 1%), or risk of treatment failure (RD –1%; 95% CI –4% to 2%) (2) . There was a reduced risk of CSF culture positivity after 10–48 hours (RD –6%; 95% CI –11% to 0%) and an increased risk of diarrhoea (RD 8%; 95% CI 3% to 13%) for third-generation cephalosporins compared with penicillin/ampicillin-chloramphenicol (2). A 2009 systematic review compared short-course (4–7 days) and long-course (7–14 days) antibiotics in children (5 RCTs; 426 patients) and found no difference in clinical success (odds ratio (OR) 1.24; 95% CI 0.73–2.11), long-term neurological complications (OR 0.60: 95% CI 0.29–1.27) or long-term hearing impairment (OR 0.59; 95% CI 0.28–1.23) (3).

Guidelines

The National Institute for Health and Care Excellence (NICE) guidelines recommend ceftriaxone for patients aged 3 months and older, while younger infants should be treated with IV cefotaxime plus amoxicillin or ampicillin (4). It is also recommended that vancomycin be added for patients who have received prolonged or multiple exposures to antibiotics within the previous 3 months and for those who have recently travelled outside the United Kingdom. IDSA (Infectious Diseases Society of America) guidelines recommend ampicillin and cefotaxime or an aminoglycoside for children less than 1 month of age, vancomycin and ceftriaxone or cefotaxime for children older than 23 months and adults up to 50 years of age, and addition of ampicillin for patients over 50 years for coverage of Listeria monocytogenes (5). Vancomycin plus cefepime, ceftazidime or meropenem is recommended for patients with penetrating trauma, who are post-neurosurgery or have a cerebrospinal shunt in place.

Rationale for antibiotic selection

Systematic review evidence suggests that chloramphenicol is associated with higher mortality than other antibiotics; it was therefore not proposed as a core antibiotic. Ampicillin, ceftriaxone and cefotaxime are proposed for multiple indications and are categorized as core, while aminoglycosides and vancomycin have more specific indications (e.g. by age or indication) and are therefore categorized as targeted, as are ceftazidime and meropenem.

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 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. Ceftazidime, amikacin, gentamicin and vancomycin were excluded, because the Committee considered that these antibiotics have limited or no indications in community-acquired acute bacterial meningitis. The Committee recommended the inclusion of chloramphenicol as a second-choice option, particularly for epidemic bacterial meningitis. Recommended first- and second-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: Bacterial meningitis

First choice	Second choice

cefotaxime

ceftriaxone

cefotaxime

ceftriaxone

ampicillin

benzylpenicillin

amoxicillin

chloramphenicol

amoxicillin

ampicillin

benzylpenicillin

chloramphenicol

1. Eliakim-Raz N, Lador A, Leibovici-Weissman Y, Elbaz M, Paul M, Leibovici L. Efficacy and safety of chloramphenicol : joining the revival of old antibiotics? Systematic review and meta-analysis of randomized controlled trials. J Antimi crob Chemother. 2015;70(4):979–96.
2. Prasad K, Kumar A, Gupta PK, Singhal T. Third generation cephalosporins versus conventional antibiotics for treati ng acute bacterial meningitis. Cochrane Database Syst Rev. 2007;(4):CD001832.
3. Karageorgopoulos DE, Valkimadi PE, Kapaskelis A, Rafailidis PI, Falagas ME. Short versus long duration of antibioti c therapy for bacterial meningitis: a meta-analysis of randomised controlled trials in children. Arch Dis Child. 2009;9 4(8):607–14.
4. Visintin C, Mugglestone MA, Fields EJ, Jacklin P, Murphy MS, Pollard AJ et al. Management of bacterial meningitis a nd meningococcal septicaemia in children and young people: summary of NICE guidance. BMJ. 2010;340:c3209.
5. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM et al. Practice guidelines for the manageme nt of bacterial meningitis. Clin Infect Dis. 2004;39(9):1267–84.

