Cefalexin

Essential medicine status ✓

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

EMLc | ATC codes: J01DB01

Indication	Bacterial cellulitis, erysipelas or lymphangitis ICD11 code: 1C00
INN	Cefalexin
Medicine type	Chemical agent
Antibiotic groups	A ACCESS
List type	Core
Formulations	Oral > Liquid: 125 mg per 5 mL (anhydrous) powder for oral liquid ; 250 mg per 5 mL (anhydrous) powder for oral liquid Oral > Solid: 250 mg (as monohydrate) ; 500 mg (as monohydrate) (EML)
EML status history	First added in 2017 (TRS 1006) Changed in 2021 (TRS 1035)
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	Cefalexin
DrugBank	Cefalexin (Cephalexin)

Expert Committee recommendation

1. Application to change the listing of cefalexin for the indication of skin and soft tissue infections from a second-choice to first-choice empiric treatment option. The Expert Committee noted that cefalexin has a spectrum of activity against pathogens responsible for mild to moderate skin and soft tissue infections which is comparable to amoxicillin + clavulanic acid and cloxacillin. The Committee considered that cefalexin as a first-generation cephalosporin is also an appropriate alternative first-choice treatment option for these infections. The Committee therefore recommended that the listing for cefalexin on the EML and EMLc be amended from a second-choice to a first-choice treatment option for mild to moderate skin and soft tissue infections. 2. Application to include new higher strength formulations of various antibiotics currently included on the EML to better align with the dosing needs of adults. The Expert Committee recommended the addition of the new strength formulations of amoxicillin, cefalexin, ceftriaxone, ciprofloxacin, clindamycin, phenoxymethylpenicillin and vancomycin to the existing listings of these medicines on the EML for the indications for which they are proposed. The Committee noted that the proposed strength formulations are higher than those currently included on the Model List, and are appropriate and aligned to meet recommended doses for treatment of adults, with the advantages of a reduced pill burden in the case of oral formulations, and facilitating a simplified and safer dose administration in the case of intravenous formulations. 3. Review of square box listings on the EML and EMLc. Following the review of square box listings on the EML and EMLc, the Expert Committee recommended that medicines in 4th level ATC chemical subgroup, J01CF Beta-lactamase resistant penicillins, be specified as therapeutic alternatives under the square box listing for cloxacillin on the EML and EMLc for skin and soft tissue infections.

Background

1. Application to change the listing of cefalexin for the indication of skin and soft tissue infections from a second-choice to first-choice empiric treatment option. Cefalexin was recommended as a second-choice treatment option on the EML and EMLc for empiric treatment of skin and soft tissue infections in adults and children in 2017, as part of the comprehensive review of antibiotics for common infectious syndromes (1). Amoxicillin + clavulanic acid and cloxacillin were recommended as first-choice treatment options because both provide good coverage against staphylococcal (non-methicillin-resistant Staphylococcus aureus (non-MRSA)) and streptococcal infections, which are the leading causes of mild to moderate community-acquired skin and soft-tissue infections worldwide. Cefalexin was recommended as second-choice for when first-choice options are not available or in patients allergic to penicillin who can tolerate cephalosporins. Bacterial skin infections occur worldwide and can affect all age groups; erysipelas is more frequent in children and elderly patients. In 2013, skin diseases (not limited to bacterial infections) were the fourth leading cause of disability worldwide (2). Cellulitis, the most common skin infection, accounted for 0.04% (4 in 10 000) of the overall burden of all diseases combined in 2013. It was the only skin condition that showed a significant decrease (–13.2%) in disability-adjusted life years (a proxy for morbidity and mortality) between 2005 and 2013; this decrease was attributed to reduced mortality (2). In 2017, the Global Burden of Disease study reported 43 million new cases of cellulitis worldwide (3). Diabetes, peripheral arterial disease, HIV infection and other causes of immunosuppression are risk factors for severe skin infections. 2. Application to include new higher strength formulations of various antibiotics currently included on the EML to better align with the dosing needs of adults. The application requested the inclusion of new higher strengths of the following antibiotics on the EML to better align with the dosing needs of adults: Amoxicillin: solid oral dosage form 1 g Cefalexin: solid oral dosage form 500 mg Ceftriaxone: powder for injection 2 g Ciprofloxacin: solid oral dosage form 500 mg Clindamycin: injection 600 mg/4 mL, 900 mg/6 mL Phenoxymethylpenicillin: tablet 500 mg Vancomycin: powder for injection 500 mg, 1 g All of the antibiotics for which additional strength formulations are proposed are currently included on the EML is various other formulations and strengths for the indications described below (1).

Summary of evidence

1. Application to change the listing of cefalexin for the indication of skin and soft tissue infections from a second-choice to first-choice empiric treatment option. Evidence of the benefits of empiric use of cefalexin for skin and soft tissue infections was reviewed and accepted by the Expert Committee in 2017. Cefalexin offers good coverage against staphylococcal (non-MRSA) and streptococcal infections with a range of activity and tolerability that is comparable with amoxicillin + clavulanic acid and cloxacillin, the first-choice options currently recommended in the Model Lists for skin and soft tissue infections. The application proposed that by also including cefalexin as a first-choice option, it will indicate that the three antibiotics are equally adequate options for empiric treatment of mild, community-acquired skin and soft tissue infections. However, it is noted that for skin infections associated with bite wounds, amoxicillin + clavulanic acid remains the preferred treatment option. 2. Application to include new higher strength formulations of various antibiotics currently included on the EML to better align with the dosing needs of adults. Amoxicillin: solid oral dosage form 1 g Most adult and adolescent patients with mild community-acquired pneumonia or acute bacterial sinusitis can be successfully treated with amoxicillin 1 g every 8 hours for 5 days. The proposed 1 g oral formulation will allow for a reduced pill burden to complete the course of treatment compared with the currently listed 500 mg strength formulation, and should facilitate adherence to treatment. Cefalexin: solid oral dosage form 500 mg Most adult patients diagnosed with exacerbations of chronic obstructive pulmonary disease, can be successfully treated with cefalexin 500 mg every 12 hours for 5 days. For bacterial pharyngitis and mild skin and soft tissue infections, most adult and adolescent patients can be successfully treated with cefalexin 500 mg every 8 hours for 5 days. The proposed 500 mg oral formulation will allow for a reduced pill burden to complete a course of treatment compared with the currently listed 250 mg strength formulation, and should facilitate adherence to treatment. Ceftriaxone: powder for injection 2 g This higher strength formulation is preferable for the treatment of certain infections because it maximizes the chances of bacterial eradication in order to achieve clinical success. For example, in the case of acute bacterial meningitis, a ceftriaxone dose of 2 g every 12 hours is needed to achieve adequate concentrations of the drug in the central nervous system. The recommended duration of treatment is 10 days. For adult patients with hospital-acquired pneumonia and no risk factors for multidrug-resistant infections, ceftriaxone 2 g a day for 7 days is a recommended treatment regimen. For complicated intra-abdominal infections, ceftriaxone 2 g per day for 5 days (in combination with metronidazole) is a recommended treatment in cases where extended-spectrum beta-lactamase strains are not suspected. For severe cases of enteric fever, if ceftriaxone is used, a dose of 2 g per day for 10 days is recommended. Ciprofloxacin: solid oral dosage form 500 mg The proposed higher strength formulation will benefit adult and adolescent patients prescribed ciprofloxacin for infections including acute

invasive bacterial diarrhoea, cholera, complicated intra-abdominal infections, enteric fever, low-risk febrile neutropenia and upper urinary tract infections. Treatment regimens recommend ciprofloxacin doses of 500 mg every 12 hours for 3, 5 or 7 days, depending on the indication or, in the case of cholera, a single dose of 1 g. The proposed 500 mg oral formulation will allow for a reduced pill burden to complete the course of treatment compared with the currently listed 250 mg strength formulation, and should facilitate adherence to treatment. Clindamycin: injection 600 mg/4 mL, 900 mg/6 mL The higher strength formulations of clindamycin are preferable for the treatment of bone and joint infections to maximize the chance of bacterial eradication in order to achieve clinical success. For adults and adolescents diagnosed with osteomyelitis, clindamycin is an acceptable treatment option when methicillin-resistant Staphylococcus aureus (MRSA) is suspected or confirmed when antimicrobial susceptibility of MRSA to clindamycin is proven or likely. Intravenous clindamycin at a dose of 600 mg every 8 hours for 4–6 weeks is a recommended dosage regimen in most cases. Clindamycin may also be used in patients allergic to penicillin. Phenoxymethylpenicillin: solid oral dosage form 500 mg Most adult and adolescent patients with mild community-acquired pneumonia, bacterial pharyngitis or dental infections can be successfully treated with phenoxymethylpenicillin 500 mg every 6 hours for 5 days; however, a longer treatment duration may be recommended in some circumstances. The proposed 500 mg strength oral formulation will allow for a reduced pill burden to complete the course of treatment compared with the currently listed 250 mg strength formulation and should facilitate adherence to treatment. Vancomycin: powder for injection 500 mg, 1 g For adult and adolescent patients with high-risk febrile neutropenia when MRSA infection is suspected, weight-based dosing of vancomycin is recommended (15–20 mg/kg every 12 hours). The 500 mg and 1 g strength formulations will allow for the achievement of recommended dose using fewer vials, compared with the currently listed 250 mg strength.

Committee considerations

2. Application to include new higher strength formulations of various antibiotics currently included on the EML to better align with the dosing needs of adults. All proposed formulations are approved by several regulatory agencies including the US Food and Drug Administration and European Medicines Agency, and are available in most countries.

EML recommendations: Bacterial cellulitis, erysipelas or lymphangitis

First choice	Second choice
amoxicillin + clavulanic acid	
cloxacillin	
cefalexin	

1. Application to change the listing of cefalexin for the indication of skin and soft tissue infections from a second-choice to first-choic e empiric treatment option.

1. The selection and use of essential medicines. Report of the WHO Expert Committee, 2017 (including the 20th WHO Model List of Essential Medicines and the 6th WHO Model List of Essential Medicines for Children). Geneva: World Health Organization. (WHO T echnical Report Series, No. 1006); 2017; https://apps.who.int/iris/handle/10665/259481, accessed 13 August 2021).
2. Karimkhani C, Dellavalle RP, Coffeng LE, Flohr C, Hay RJ, Langan SM, et al. Global skin disease morbidity and mortality: an update f rom the Global Burden of Disease Study 2013. JAMA Dermatol. 2017;153(5):406–12.
3. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and ye ars lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Glo bal Burden of Disease Study 2017. Lancet. 2018;392(10159):1789–858.

2. Application to include new higher strength formulations of various antibiotics currently included on the EML to better align with th e dosing needs of adults.

1. WHO Model List of Essential Medicines. 21st List. Geneva, World Health Organization; 2019. (https://apps.who.int/iris/handle/1 0665/330668, accessed 13 August 2021).