The Expert Committee endorsed the inclusion on the EMLc of amoxicillin as a first-choice therapy for use in uncomplicated severe acute malnutrition, and of benzylpenicillin or ampicillin and gentamicin followed by amoxicillin as first-choice therapy in use in complicated severe acute malnutrition.

Severe acute malnutrition (SAM) affects nearly 20 million children under 5 years of age, causing up to 1 million deaths each year as a consequence of increasing susceptibility to death from severe infection (1). The most susceptible age for malnutrition is 6–18 months, but it is increasingly recognized that SAM may occur in younger infants (2). SAM is classified according to the absence or presence of medical complications (3): • Uncomplicated SAM: children who are clinically well without signs of infection or other indication for hospital admission, with a retained appetite (“passed the appetite test”). Retained appetite is regarded as indicating the absence of severe metabolic disturbance. Patients are deemed to be most appropriately managed as outpatients, with ready-to-use therapeutic foods. • Complicated SAM: children who have clinical features of infection, metabolic disturbance, severe oedema, hypothermia, vomiting, severe dehydration, severe anaemia or a lack of appetite, requiring inpatient treatment initially with low-protein milk-based feeds. Children are discharged to continue nutritional management as outpatients when complications have resolved. The following summary is taken from the review of the available evidence for SAM conducted to inform the WHO Department of Maternal, Newborn, Child and Adolescent Health’s review of its existing guidelines.
Summary of evidence

A comprehensive search for systematic reviews, meta-analyses, multicentre studies and randomized controlled trials was conducted. Seven studies were included in the final analysis: four systematic reviews and/or meta-analyses (4–7) and three double-blind, placebo-controlled trials (8–10). The meta-analysis by Million et al. (7) found an overall benefit for survival in children with SAM treated with amoxicillin, sufficient to reaffirm 2013 WHO recommendations (which recommend amoxicillin for children with uncomplicated SAM). Current evidence supports administration of amoxicillin 80 mg/kg per day in two divided doses for 7 days to children with SAM in the community setting. For complicated SAM, the evidence supports maintaining the existing recommendation of empirical parenteral benzylpenicillin or ampicillin plus gentamicin, followed by oral amoxicillin once the patient is clinically stable.

Guidelines

The application stated that there are significant variations in published international guidelines for the suggested antimicrobial therapies for empirical antimicrobial treatment of complicated SAM, many of which pre-date recent trials. The 2013 WHO guidelines for treatment of SAM (3) make the following recommendations regarding antibiotic treatment of SAM: • Children with uncomplicated SAM, not requiring to hospital admission and managed as outpatients, should be given a course of oral antibiotic such as amoxicillin (conditional recommendation, low-quality evidence). • Children who are undernourished but do not have SAM should not routinely receive antibiotics unless they show signs of clinical infection (strong recommendation, low-quality evidence). • Children admitted with SAM and complications such as septic shock, hypoglycaemia, hypothermia, skin infections or respiratory or urinary tract infections, or who appear lethargic or sickly, should be given parenteral (IM or IV) antibiotics. • Children admitted with SAM and with no apparent signs of infection and no complications should be given an oral antibiotic.

Rationale for antibiotic selection

Alignment with WHO guidelines.

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 antibiotics proposed in the application from the WHO Department of Maternal, Newborn, Child and Adolescent Health, and selected first-choice antibiotics for inclusion on the EMLc for this indication in alignment with the WHO guidelines. Second-choice therapies were neither proposed nor recommended. Recommended first-choice antibiotics for uncomplicated and complicated SAM are reported above.

EML recommendations: Acute malnutrition in infants, children or adolescents

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<tr>
<th>First choice</th>
<th>Second choice</th>
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<tr>
<td><strong>UNCOMPROMICATED [CHILDREN]</strong></td>
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<td>amoxicillin</td>
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<td><strong>COMPLICATED [CHILDREN]</strong></td>
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amoxicillin

benzylpenicillin

co-prescribed with gentamicin

ampicillin

co-prescribed with gentamicin