Vancomycin

**Section:** 6. Anti-infective medicines > 6.2. Antibacterials > 6.2.2. Watch group antibiotics

- **Indication:** Necrotising fasciitis
- **ICD11 code:** 1B71.2
- **INN:** Vancomycin
- **Medicine type:** Chemical agent
- **Antibiotic groups:** WATCH
- **List type:** Complementary
- **Formulations:** Parenteral > General injections > IV: 250 mg in vial (as hydrochloride) powder for injection; 500 mg in vial (as hydrochloride) powder for injection (EML); 1 g in vial (as hydrochloride) powder for injection (EML)
- **EML status history:** First added 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.

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**Wikipedia**
Vancomycin

**DrugBank**
Vancomycin

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**Expert Committee recommendation**

The Expert Committee noted that necrotizing fasciitis is a rare but severe skin and soft tissue infection that is associated with significant morbidity and mortality, especially in cases of delayed diagnosis and treatment. The Committee noted the previous decision not to include empiric antibiotic treatment for severe skin and soft tissue infections, and to focus rather on mild, community-acquired infections. However, given the serious consequences of delayed treatment in necrotizing fasciitis, the Committee considered recommendations for empiric antibiotic therapy would be beneficial from both a clinical and public health perspective. The Expert Committee reviewed the antibiotics proposed for listing for necrotizing fasciitis in the 2017 application and recommended expanding the indications for ceftriaxone, clindamycin, metronidazole, piperacillin + tazobactam and vancomycin on the EML and EMLc to include them as first-choice treatment options for treatment of necrotizing fasciitis as proposed in the application, including the addition of new intravenous formulations of ceftriaxone 2 g, clindamycin 600 mg and 900 mg, and vancomycin 500 mg and 1 g.

**Background**

Ceftriaxone, clindamycin, metronidazole, piperacillin + tazobactam and vancomycin are currently included in the EML and EMLc for multiple other indications. A review of antibiotic treatment for skin and soft tissue infections was prepared by the Department of Health Research Methods, Evidence and Impact, McMaster University, Canada and was considered by the Expert Committee in 2017. The Committee recommended listing amoxicillin + clavulanic acid, cloxacillin and cefalexin for the treatment of mild skin and soft-tissue infections. The antibiotics proposed in the application for severe skin and soft-tissue infections (including necrotizing fasciitis) were not recommended because the Committee chose to focus on the empirical treatment of common mild to moderate community-acquired infections (1). Necrotizing fasciitis is a rare infection, but it is associated with significant morbidity and
mortality, especially in cases of delayed diagnosis and treatment. The disease is caused mostly by bacteria and is characterized by acute and fulminant necrosis with tissue destruction and signs of systemic toxicity. Risk factors for necrotizing fasciitis include traumatic and surgical wounds, especially in patients with diabetes, peripheral vascular disease or immunosuppression (2). However, necrotizing fasciitis can also occur in otherwise healthy people irrespective of their age. Necrotizing fasciitis is very rare in children but may occur as a complication of varicella (chickenpox) or in the context of a compromised immune system. Few data are available on time trends in the epidemiology of necrotizing fasciitis. In the USA, over a 10-year period (2003–2013), an estimated 9871 deaths related to necrotizing fasciitis occurred, corresponding to a mortality rate of 4.8 per million person-years (3). In an Asian study, an overall annual incidence of 3.2 hospitalizations per 100 000 person-years was reported between 2002 and 2011 (4). Other studies report an incidence that ranges from 0.3 to 15 cases per 100 000 population (2,5,6). Among all invasive Streptococcus pyogenes infections, necrotizing fasciitis represents only a minority of cases – about 7% for all ages combined in one study of surveillance data in the USA (7).

### Summary of evidence

The 2017 McMaster review of systematic reviews, meta-analyses and guidelines published between 1996 and 2016 for antibiotics for skin and soft tissue infections included evidence for antibiotic treatment of severe skin and soft tissue infections, and is summarized in the report of the 2017 Expert Committee meeting (1). Since no important new evidence on antibiotic therapeutic options for this infection has become available since then, the evidence presented in 2017 still reflects the current evidence base. The 2017 review included the 2014 guidelines of the Infectious Diseases Society of America on skin and soft tissue infections, which cover both paediatric and adult patients (8). These guidelines included the following recommendations for necrotizing infections of the skin, fascia and muscle: (i) piperacillin + tazobactam plus vancomycin; (ii) a carbapenem (meropenem, imipenem, ertapenem), or (iii) cefotaxime plus metronidazole or clindamycin. Antibiotics, including cefazolin, ceftriaxone, clindamycin, daptomycin, doxycycline, linezolid, penicillin G, quinupristin + dalfopristin, semi-synthetic penicillins (nafcillin, oxacillin) and vancomycin, and are listed as options for specific pathogens such as Streptococcus, Staphylococcus aureus, Clostridium species, Aeromonas hydrophila and Vibrio infections. In the context of the 2017 McMaster review, ceftriaxone, clindamycin, meropenem, metronidazole, piperacillin + tazobactam and vancomycin were proposed as treatment options for severe skin and soft tissue infections (including necrotizing fasciitis) for inclusion on the Model Lists. The Expert Committee did not recommend them because it decided to prioritize listing of antibiotics for mild, community-acquired infections. Therefore, the Expert Committee’s decision was not a reflection of its evaluation of the evidence for benefit for these antibiotics in the treatment of necrotizing fasciitis. Ceftriaxone, clindamycin, metronidazole, piperacillin + tazobactam and vancomycin are already included in the EML and EMLc. They are widely used for many different types of infection and potential side-effects when used for the treatment of necrotizing fasciitis do not differ from those encountered when these antibiotics are used for a different indication. Given the severity of necrotizing fasciitis and the high mortality associated with delays in treatment, the benefits of adequate antibiotic treatment outweigh the potential side-effects of each individual antibiotic.

### Guidelines

There are no WHO guidelines for the management of severe skin and soft tissue infections and necrotizing fasciitis.

### Rationale for antibiotic selection

Following the principles of antimicrobial stewardship, meropenem has not been generally recommended as an option for the empiric treatment of clinical infections. Wide use of empiric treatment with meropenem has been associated with selection of carbapenem resistance at both a patient and hospital level. Recommendations for the use of meropenem have generally been limited to where a patient is known to be infected or colonized with a multidrug-resistant pathogen that is resistant to other recommended antibiotics.

### Committee considerations

Dose forms and strengths as currently listed on the EML and EMLc, plus additional new strength intravenous formulations for ceftriaxone, clindamycin and vancomycin on the EML to better meet the dosing needs of adults for this indication. Ceftriaxone: powder for injection 2 g Clindamycin: injection 600 mg/4 mL and 900 mg/6 mL Vancomycin: powder for injection 500 mg and 1 g As the proposed medicines are already included on the Model Lists and on many national essential medicine lists, a review of the
comparative costs and cost-effectiveness was not done. Ceftriaxone, clindamycin, metronidazole, piperacillin + tazobactam and vancomycin have regulatory approval globally and generic varieties are available.

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