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I.5 - Proposal for the inclusion of ceftriaxone, clindamycin, metronidazole, piperacillin-tazobactam and vancomycin on the WHO Model List of Essential Medicines and the WHO Model List of Essential Medicines for Children for the new indication of necrotizing fasciitis.

MSF supports the addition of the new indication of necrotizing fasciitis to the existing indications listed for ceftriaxone, clindamycin, metronidazole, piperacillin-tazobactam and vancomycin in the core list in section 6.2 Antibacterials in both the WHO Model List of Essential Medicines (EML) and the WHO Model List of Essential Medicines for Children (EMLc).

MSF welcomes the rigorous and comprehensive review already presented for the 2017 update of the EML and the proposal for alignment on recommendations currently existing in several guidelines and documents, for the treatment of severe community-acquired skin and soft tissue infections.

Necrotizing fasciitis is a rare and life-threatening subcutaneous soft-tissue infection, polymicrobial due to mixed anaerobic/facultative anaerobic organisms, or monomicrobial commonly due to *Streptococcus pyogenes*. Symptoms are acute and fulminant necrosis with tissue destruction, associated with signs of systemic toxicity (fever, tachycardia, hypotension, shock). Necrotizing fasciitis is associated with a high rate of morbidity and mortality, depending on the promptness of diagnosis and treatment. Antibiotic therapy is crucial, but is considered adjunctive to surgical management.

Ceftriaxone is included since 1995, clindamycin since 1991, metronidazole since 1977, piperacillin + tazobactam since 2017 and vancomycin since 1995, in the WHO Model List of Essential Medicines, for various indications of infections.

Ceftriaxone, piperacillin-tazobactam and vancomycin are listed in section 6.2.2 Watch group antibiotics, while clindamycin and metronidazole are listed in section 6.2.1 Access group antibiotics.

The 2018 “World Society of Emergency Surgery and Surgical Infection Society Europe recommendations for the management of skin and soft-tissue infections” recommend that the initial empirical antibiotic regimen should comprise broad-spectrum drugs including anti-methicillin-resistant Staphylococcus aureus (anti-MRSA) and anti-Gram-negative coverage.

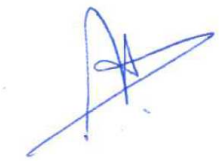
For the treatment of Gram-negative bacteria, the use of piperacillin-tazobactam is appropriate. For MRSA, vancomycin is recommended.

The 2014 update of the "Practice guidelines for the diagnosis and management of skin and soft tissue infections" by the Infectious Diseases Society of America (IDSA) recommends that empiric antibiotic treatment should use broad-spectrum antibiotics (e.g. vancomycin or linezolid plus piperacillin-tazobactam or plus a carbapenem, or plus ceftriaxone and metronidazole), as the etiology can be polymicrobial (mixed aerobic-anaerobic organisms) or monomicrobial (group A *Streptococcus*, community-acquired MRSA). Penicillin plus clindamycin is recommended for treatment of documented group A streptococcal necrotizing fasciitis.

According to the application, empiric treatment should use piperacillin-tazobactam in combination with clindamycin; ceftriaxone in combination with metronidazole should be used only after *Streptococcus pyogenes* necrotizing fasciitis has been ruled out and if MRSA is suspected, vancomycin should be used in combination with one of the above-mentioned combination. Piperacillin-tazobactam is the only antibiotic listed in the application to have antipseudomonal activity. To better serve the needs for treatment of necrotizing fasciitis in adults, new formulations of ceftriaxone (2 g powder for injection), clindamycin (600 mg and 900 mg) and vancomycin (500 mg and 1 g) should be added to the already listed formulations of these antibiotics in the EML.

MSF urges the 23rd Expert Committee on the Selection and Use of Essential Medicines to add the indication of necrotizing fasciitis to the existing indications listed for ceftriaxone, clindamycin, metronidazole, piperacillin-tazobactam and vancomycin, and also to add the above-mentioned new formulations, in the core list in section 6.2 Antibacterials in the WHO Model List of Essential Medicines and in the WHO Model List of Essential Medicines for Children.

For Médecins Sans Frontières



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