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A.44 Tedizolid phosphate. Powder for intravenous injection 200 mg vial and oral tablet, 200 mg.

MSF supports the inclusion of tedizolid phosphate in Section 6.2.3 "Reserve group antibiotics" in the WHO Model List of Essential Medicines (EML).

Tedizolid phosphate is a novel oxazolidinone antibacterial agent that inhibits mitochondrial protein synthesis, has *in-vitro* activity against susceptible Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA) and some MRSA strains resistant to linezolid, or those with reduced susceptibility and/or resistance to vancomycin. In the USA and in Europe, tedizolid phosphate is indicated for the treatment of acute bacterial skin and skin structure infections in adults and adolescents 12 years of age and older.

Both IV and oral formulation of tedizolid are recommended in the management of MRSA skin and soft-tissue infections by the Surgical Infection Society (SIS) guidelines[1] and in a consensus statement published by the World Society of Emergency Surgery (WSES) and the Surgical Infection Society Europe (SIS-E)[2].

MSF would like to draw the attention of the Expert Committee on the following facts:

- MSF faces patients with infections by methicillin-resistant *Staphylococcus aureus* (MRSA) and some MRSA strains resistant to linezolid in MSF and MSF supported hospitals, e.g. in the Middle East. In MSF contexts, tedizolid is an option for the treatment of skin/soft tissue infections with MRSA, vancomycin-intermediately susceptible (VISA) and some linezolid-resistant *Staphylococcus aureus* isolates.

- Tedizolid phosphate is approved by the FDA and the EMEA for the treatment of acute bacterial skin and skin structures infections only, in adults and adolescents 12 years of age and older; more evidence is needed to define tedizolid's role in infections other than the above-mentioned.

- Tedizolid phosphate presents the advantages of a low potential for clinically significant drug-drug interactions, no dose adjustment nor monitoring in renal impairment, hepatic impairment, obese patients and elderly patients. Oral bioavailability of tedizolid phosphate allows that no

[1] Duane TM, Huston JM, Collom M at al. Surgical Infection Society 2020 updated guidelines on the management of complicated skin and soft tissue infections. *Surg Infect (Larchmt).* 2021;22:383-399.
[2] Sartelli M, Guirao X, Hardcastle TC et al. 2018 WSES/SIS-E consensus conference: recommendations for the management of skin and soft-tissue infections. World J Emerg Surg. 2018 Dec 14;13:58.

dose adjustment is required when switching from IV route to oral route and a once-daily oral dosing, facilitating early hospital discharge.

- MSF highlights that oral options with high bioavailability and favourable side effect/interaction profiles are lacking. MSF notices that data regarding efficacy and tolerability for use in the treatment of osteomyelitis are insufficient[3] [4] [5] [6] [7] [8]. Alternative to linezolid (or rifampicin) for treatment of MDR gram positives pathogens for osteomyelitis is urgently needed.

- Tedizolid phosphate is registered in 43 highly regulated countries. Currently, access is impossible in most resource limited settings due to prohibitive prices and lack of registration, barriers which should be worked on to guarantee that all patients in need can benefit (together with microbiology laboratory support for diagnosis). MSF emphasized that actions to foster access are sorely needed given very high prices and limited number of countries where tedizolid phosphate is registered.

- The inclusion of tedizolid phosphate in the EML will serve as a basis for National Essential Medicines lists and therefore will motivate additional manufacturers, particularly in low- and middle-income countries.

In light of this elements, MSF urges the 24th Expert Committee on the Selection and Use of Essential Medicines to consider the inclusion of tedizolid phosphate in Section 6.2.3 “Reserve group antibiotics” in the WHO Model List of Essential Medicines.

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[3] Bloem, Annemieke et al. “New-Generation Antibiotics for Treatment of Gram-Positive Infections: A Review with Focus on Endocarditis and Osteomyelitis.” *Journal of clinical medicine* vol. 10,8 1743. 17 Apr. 2021
[4] Carvalhaes CG, Sader HS, Flamm RK, Mendes RE. Tedizolid in vitro activity against Gram-positive clinical isolates causing bone and joint infections in hospitals in the USA and Europe (2014-17). *J Antimicrob Chemother*. 2019;74(7):1928-1933.
[5] Mensa Vendrell M, Tasias Pitarch M, Salavert Lletí M, et al. Safety and Tolerability of More than Six Days of Tedizolid Treatment. *Antimicrob Agents Chemother*. 2020;64(7):e00356-20.
[6] Park KH, Greenwood-Quaintance KE, Schuetz AN, Mandrekar JN, Patel R. Activity of Tedizolid in Methicillin-Resistant Staphylococcus epidermidis Experimental Foreign Body-Associated Osteomyelitis. *Antimicrob Agents Chemother*. 2017;61(2):e01644-16.
[7] Ueda T, Nakajima K, Ichiki K, et al. Correction of thrombocytopenia caused by linezolid with scheduled sequential tedizolid use in patients with vertebral osteomyelitis by antibiotic resistant Gram-positive organisms. *J Infect Chemother*. 2022;28(7):1023-1028.
[8] Park KH, Greenwood-Quaintance KE, Mandrekar J, Patel R. Activity of Tedizolid in Methicillin-Resistant Staphylococcus aureus Experimental Foreign Body-Associated Osteomyelitis. *Antimicrob Agents Chemother*. 2016;60(11):6568-6572