A.44	Tedizolid phosphate – bacterial infections due to multidrug-resistant organisms – EML
Draft recommendation	☒ Recommended – square box ☐ Not recommended Justification: Tedizolid is an oxazolidinone antibiotic in the same class as linezolid, which is on the Reserve List of the EML/c. It is active against Gram positive infections, mainly *Staphylococcus aureus* particularly focussed on the treatment of methicillin resistant (MRSA) skin and soft tissue infections. Tedizolid is licenced by the FDA and EMA for the treatment of Acute Bacterial Skin and Skin Structure Infection (ABSSSI) in adults. MRSA causing severe bacterial infections remain a major global public health concern, with significant mortality associated with invasive disease. The ESTABLISH 1 and 2 trials compared both oral, and intravenous with oral step down, tedizolid and linezolid regimens in adults with ABSSSI. Very similar rates of early and late clinical response were noted. Lower rates of bone marrow suppression and gastro-intestinal symptoms were noted in the tedizolid arms. Tedizolid was dosed once daily for 6 days compared to linezolid given twice daily for 10 days. Tedizolid dosing adjustment is not required for renal or hepatic failure. Tedizolid has a considerably higher costs compared to other oral generic antibiotics used to treat skin infections. Limited cost effectiveness data is available from LMIC settings.
Does the proposed medicine address a relevant public health need?	☒ Yes ☐ No ☐ Not applicable Comments: MRSA remains a leading cause of mortality globally, and SA was one of the 5 leading pathogens associated with infection-related deaths in the GRAM study (Lancet 2023).
Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (this may be evidence included in the application, and/or additional evidence identified during the review process)	☒ Yes ☐ No ☐ Not applicable Comments: The ESTABLISH 1 trial compared 6 days of once daily oral tedizolid to 10 days of oral twice daily linezolid in 667 adults with ABSSSI. Non-inferiority was demonstrated for both early and late clinical outcomes and were similar in the 178 patients where MRSA had been isolated from the primary lesion. In the ESTABLISH 2 trial tedizolid was given intravenously, with an optional oral step down for a total of 6 days, again compared to ten days of linezolid. Non-inferiority was demonstrated, with very similar clinical response seen in both arms.

Does adequate evidence exist for the safety/harms associated with the proposed medicine? (this may be evidence included in the application, and/or additional evidence identified during the review process)	☒ Yes ☐ No ☐ Not applicable Comments: Tedizolid was well tolerated with largely minor adverse events noted in the above trials. Many antibiotics cause bone marrow suppression, but high rates of neutropenia and thrombocytopaenia have particularly been associated with linezolid use. Significantly lower rates of marrow suppression were noted in the tedizolid arms of the ESTABLISH trials, as well as lower rates of gastro-intestinal symptoms.
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments: Tedizolid does not require dose adjustment in patients with renal or hepatic disease.
Are there any special requirements for the safe, effective and appropriate use of the medicines? (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☒ Yes ☐ No ☐ Not applicable Comments: Patients who develop myelosuppression should be re-evaluated and if treatment is continued, regular blood count monitoring is recommended.
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☒ Yes ☐ No ☐ Not applicable Comments: Tedizolid is a high cost drug compared to most other oral antibiotics treating skin infections on the EML. However, the BNF 2023 notes 6 days of tedizolid to be a similar cost compared to generic linezolid given orally twice daily for 10 days. Limited cost effectiveness data is available.
Are there any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable Comments: The application notes that tedizolid is licensed in 43 countries globally.

Is the proposed medicine recommended for use in a current WHO guideline? (refer to: https://www.who.int/publications/who-guidelines)	☐ Yes ☒ No ☐ Not applicable Comments: Linezolid is listed on the EML/c as a Reserve antibiotic, but because of the absence of informative comparator data no formal recommendation is given on its use.