Linezolid – therapeutic drug monitoring

Linezolid is an oxazolidinone antibiotic. It is used for the treatment of severe infections caused by resistant Gram-positive bacteria, such as vancomycin-resistant enterococci (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA) and has an emerging role in treating non-tuberculous mycobacterial infections. This guide will give recommendations for therapeutic drug monitoring (TDM) of Linezolid for the treatment of gram-positive infection. **TDM of Linezolid in mycobacterium infection is not discussed in this guide**.

Key concepts

- Serum Linezolid levels are indicators of both efficacy and safety.
- Duration of therapy > 2 weeks is associated with development of thrombocytopenia
- Adverse events include myelosuppression (thrombocytopenia, anemia), lactic acidosis, and peripheral and optic neuropathy
- Multiple possible drug-drug interactions (check before use)

Indication for TDM (any of the following):

- Anticipated duration of therapy > 10 days
- Any duration in patients with pre-existing thrombocytopenia
- Any duration in patients with significant risk for sub- or supratherapeutic drug levels, such as :
    - Age >70y
    - BMI ≤20 or ≥30
    - Altered kidney function: eGFR ≤ 40ml/min (including dialysis patient) or ≥130ml/min
    - Severe liver impairment (Child-Pugh grade C)
    - Other conditions likely to cause PK changes (e.g. cystic fibrosis, critically ill patients, pregnancy, ECMO and malabsorption risk)
- After any TDM-guided dosing change
- Suspected treatment failure (non-resolving infections) or non-compliance
- Suspected hematologic or neurologic drug toxicity

Target serum level, timing and frequency of TDM

- **Trough target (pre-level): 2 - 7mg/L** (For long term use, aim for lower end of the range)
- Collect blood 48h after treatment start or dose modification, 30-60 minutes pre-next dose.
- Once target reached, weekly TDM until end of therapy (expect delays in results, tests are sent out)
    - Instructions on how to draw blood available here (section analysis then enter Linezolid in search engine)
- Other monitoring: CBC, chem7, LFTs 2-3 times per week in hospital, at least weekly in outpatient

Dosage adjustment

- Linezolid exhibits predominantly linear elimination. Oral and IV doses are equivalent.
- If trough level < 2mg/L in patient on 600mg po/IV q12h:
    - Increasing to 450mg PO/IV q8h and recheck trough concentrations after 48 hours.
    - If still < 2, increase to 600mg po/IV q8h
- If trough level > 8mg/L and patient on 600mg po/IV q12h:
    - Decrease to 600mg po/IV die and recheck level after 48h
    - If still >8, decrease to 300mg po/IV die

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