Linezolid
Newborn use only

2020

Alert	Linezolid is not the standard first-line therapy for treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) or coagulase-negative staphylococci (CoNS).[1] Antimicrobial stewardship team recommends this drug as restricted.
Indication	Treatment of Gram-positive infections either refractory to vancomycin or where vancomycin is contraindicated.
Action	Oxazolidinone class of antibiotic that act as a protein synthesis inhibitors on the ribosomal 50S subunit of the bacteria. This prevents the formation of the 70S initiation complex which is a prerequisite for bacterial reproduction. Linezolid possesses antimicrobial activity against a wide variety of Gram-positive pathogens, with bactericidal effects against most strains of *Streptococcus spp.* and bacteriostatic action against *Enterococcus spp.* and *Staphylococcus spp.*, including VRE, MRSA and methicillin-resistant CoNS. Linezolid is also active against anaerobes, atypical microbes such as *Chlamydia* and *Mycoplasma spp.*, some rapidly growing mycobacteria and selected Gram-negative bacilli.[2]
Drug type	Oxazolidinone antibiotic.
Trade name	Zyvox, Pharmacor Linezolid, Linezolid Kabi, Linezolid APO, Linezolid Amneal, Linevox
Presentation	IV: 600 mg in 300 mL infusion preparation (2 mg/mL) Oral suspension (after reconstitution): 100 mg/5 mL (20 mg/mL)
Dose	**Standard dosing** IV or Oral Intermittent regimen[2-4] Gestation: ≤34^{+6} weeks; Postnatal age: ≤7 days; Dose: 10 mg/kg/dose every 12 hours Gestation: ≤34^{+6} weeks; Postnatal age: >7 days; Dose: 10 mg/kg/dose every 8 hours Gestation: ≥35^{+0} weeks; Postnatal age: ; Dose: 10 mg/kg/dose every 8 hours IV continuous infusion[5] 30 mg/kg/day Higher dosing (for pathogens with MIC ≥2 mg/L) 12 mg/kg/dose 8-hourly. Watch for thrombocytopenia and lactic acidosis.[3]
Dose adjustment	Therapeutic hypothermia: Not enough evidence for dose adjustment ECMO: Adult data suggest standard dosing may not be sufficient.[6,7] Renal impairment: Consider therapeutic drug monitoring and adjust accordingly[8] (refer to monitoring section) Hepatic impairment: No dose adjustment is required[8]
Maximum dose	600 mg daily
Total cumulative dose	
Route	IV or Oral
Preparation	IV infusion: Use undiluted, supplied as ready-to-use infusion Oral suspension: Add 123 mL of water for irrigation to the powder in 2 parts and shake well to make a uniform suspension. Final reconstituted volume is 150 mL to make a final concentration of 20 mg/mL.
Administration	IV: Infuse over 30 to 120 minutes or administer as a continuous infusion. Oral: Shake well before use. May be given at any time with regards to feeds.
Monitoring	Periodic full blood count, lactate and liver function test for any development of thrombocytopenia, lactic acidosis and elevated transaminases, particularly if linezolid is used for >2 weeks[3,9] For use >4 weeks, monitor for cataracts and neuropathy[10,11] Therapeutic Drug Monitoring (TDM): TDM is not routine for linezolid in Australia. To balance linezolid efficacy and toxicity, suggested target trough concentrations in clinical studies were 2–8 mg/L, 3.6–8.2 mg/L or 2–7 mg/L.[8] In Australia, linezolid TDM is available at the following laboratories: St. Vincent's Hospital (NSW) – Ph: (02) 8382 9184 and Pathology Queensland – Ph: (07) 3646 0028.
Contraindications	Hypersensitivity to linezolid or any component of the formulation (MIMS online) Monoamine oxidase inhibitors: Linezolid should not be used in patients taking any medicinal product which inhibits monoamine oxidases A or B or within two weeks of taking any such medicinal product.[12] Potential interactions producing elevation of blood pressure: Unless patients are monitored for potential increases in blood pressure, linezolid should not be administered to patients with uncontrolled

	hypertension, pheochromocytoma, thyrotoxicosis and/or patients taking any of the following types of medications: directly and indirectly acting sympathomimetic agents (e.g. pseudoephedrine), vasopressor agents (e.g. adrenaline [epinephrine], noradrenaline [norepinephrine]), dopaminergic agents (e.g. dopamine, dobutamine)[12] Potential serotonergic interactions: Unless patients are carefully observed for signs and/or symptoms of serotonin syndrome, linezolid should not be administered to patients with carcinoid syndrome and/or patients taking any of the following medications: serotonin reuptake inhibitors, tricyclic antidepressants, pethidine or buspirone.[12]
Precautions	Infants with central nervous system infections due to variable linezolid CSF concentrations.[13] Myelosuppression (including anaemia, leukopenia, pancytopenia and thrombocytopenia) and lactic acidosis have been reported commonly. Serotonin syndrome: May occur with concomitant pro-serotonergic drugs, agents which reduce linezolid's metabolism or in patients with carcinoid syndrome. Avoid use in such patients unless clinically appropriate and under close monitoring for signs/symptoms of serotonin syndrome.[8] Peripheral and optic neuropathy has been reported in adults and children and may occur primarily with extended courses of therapy >28 days.[14-16]
Drug interactions	Sympathomimetic and adrenergic agents: As a non-selective monoamine oxidase (MAO) inhibitor, linezolid can raise noradrenaline (norepinephrine) concentrations and amplify adrenergic effects. Co-administration of linezolid with sympathomimetic agents or adrenergic agonists, such as pseudoephedrine and bronchodilators, increases the risk of adverse effects, including elevated blood pressure.[17] Serotonergic drugs: Co-administering linezolid with selective serotonin reuptake inhibitors (SSRI) or other serotonergic drugs can increase the risk of serotonin toxicity due to the additive serotonergic effects of MAO inhibitors.[18] If breastfeeding mother is on any antidepressants or antipsychotics, please contact clinical pharmacist to check if it is detected in breastmilk and risk of drug interactions. Rifampin and levothyroxine can increase clearance and decrease linezolid plasma concentrations.[8] Co-administration of linezolid with amiodarone or calcium channel blockers may also result in higher linezolid exposures.[8] Linezolid may interact with warfarin to increase the international normalised ratio (INR)[8]
Adverse reactions	Thrombocytopenia and anaemia occur in 2–5%. Lactic acidosis – rare. Elevated transaminases and diarrhoea occur in 5% Cataracts are reported in preterm infants Peripheral and optic neuropathy and convulsions have been reported, mainly in patients treated for longer than 28 days
Compatibility	Sodium chloride 0.9%, gucose 5%, Ringer's lactate (Hartmann's) Y-Site: Aciclovir, adrenaline (epinephrine), alfentanil, allopurinol, amikacin, aminophylline, amiodarone, amphotericin B lipid complex/liposome, ampicillin, anidulafungin, atenolol, atracurium, azithromycin, aztreonam, calcium chloride, calcium gluconate, cefazolin, cefotaxime, ceftriaxone, chloramphenicol, ciprofloxacin, clindamycin, dexamethasone sodium phosphate, dexmedetomidine, digoxin, diltiazem, dobutamine, fentanyl citrate, fluconazole, furosemide (frusemide), gentamicin, haloperidol, heparin sodium, hydralazine, hydrocortisone, insulin, labetalol, lidocaine (lignocaine), lorazepam, magnesium sulfate, meropenem, metronidazole, midazolam, morphine sulfate, naloxone, noradrenaline (norepinephrine), phenobarbital, piperacillin/tazobactam, potassium chloride, remifentanil. rocuronium, sodium bicarbonate, sufentanil, tobramycin, vancomycin, vecuronium, verapamil , zidovudine
Incompatibility	Amphotericin B conventional, ceftriaxone, chlorpromazine, diazepam, erythromycin, pantoprazole, pentamidine, phenytoin, thiopentone sodium, trimethoprim/sulfamethoxazole
Stability	IV injection may exhibit yellow colour that can intensify over time without affecting potency. Store at 25°C. Protect from light. Suspension is stable for 21 days after reconstitution. Store at 25°C (before and after reconstitution). Protect from light.
Storage	Store at room temperature, do not freeze. Protect from light.
Excipients	IV injection: Glucose, sodium citrate, citric acid, hydrochloric acid and/or sodium hydroxide and water for injection Oral suspension: Sucrose, mannitol, microcrystalline cellulose, carmellose sodium, aspartame, anhydrous colloidal silica, sodium citrate dihydrate, xanthan gum, sodium benzoate, citric acid and sodium chloride.

	The granules are flavoured with mafco magna sweet, orange flavour, orange cream flavour, sweet-am powder, vanilla flavour and peppermint flavour.
Special comments	
Evidence	Refer to full version.
Practice points	Refer to full version.
References	Refer to full version.

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