Clindamycin
Newborn use only

2022

Alert	In the Australian context, clindamycin is not used as first line therapy for infections in neonates. Infectious Diseases consultation is recommended prior to commencement. May be used for penicillin allergic patients or other patients for whom penicillin is inappropriate, provided the target organism is also expected to be susceptible to clindamycin. Dalacin C injection contains benzyl alcohol. Avoid exposure of > 99 mg/kg/day of benzyl alcohol in neonates.[6]
Indication	Treatment of infections with susceptible organisms where first-line therapy is contraindicated or unavailable. Suitable infections may include intraabdominal infections, skin and soft tissue infections or bone and joint infections.
Action	Binds to the 50S subunit of susceptible bacterial ribosomes and inhibits protein synthesis.[1]
Drug type	Lincosamide antibiotic derived from lincomycin.
Trade name	Dalacin C, Clindamycin Mylan.
Presentation	300 mg/2 mL, 600 mg/4 mL (150 mg/mL)
Dose	**IV[2]*** *** In the Australian context, clindamycin is not used as the first line therapy for infections. Infectious Diseases consultation is recommended.**

Corrected Gestational Age/Postmenstrual Age*	Dose	Frequency
$<33^{+0}$ weeks	5 mg/kg	8th hourly
33^{+0}-40^{+6} weeks	7 mg/kg	8th hourly
$\geq 41^{+0}$ weeks	9 mg/kg	8th hourly

Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No dose adjustment is necessary. Hepatic impairment – Use with caution in severe hepatic impairment.
Maximum dose	27 mg/kg/day
Total cumulative dose	
Route	Intravenous
Preparation	Draw up 0.5 mL (75 mg) of clindamycin and add 24.5 mL of sodium chloride 0.9% or glucose 5% to make a final volume of 25 mL with a concentration of 3 mg/mL.
Administration	IV infusion over 1 hour
Monitoring	Full blood count, hepatic and renal function during prolonged treatment
Contraindications	Serious allergic reaction to clindamycin or lincomycin or to any of the inactive ingredients.
Precautions	
Drug interactions	CYP3A4 inhibitors may potentially increase the clindamycin concentrations and a risk of clindamycin toxicity.
Adverse reactions	Diarrhoea (mild-to-severe), nausea, vomiting, abdominal pain or cramps, rash, itch.
Compatibility	Fluids: Glucose 5%, glucose in sodium chloride solutions, sodium chloride 0.9%, Y-site[7]: Aciclovir, amikacin sulfate, aztreonam, cephamandole nafate, calcium chloride, cefazolin sodium, cefotaxime, cefoxitin, ceftazidime, ceftizoxime, dexamethasone, dexmedetomidine, digoxin, dopamine, ephedrine sulfate, fentanyl, furosemide, heparin sodium, hydrocortisone sodium succinate, gentamicin, morphine sulfate, noradrenaline (norepinephrine), paracetamol, netilmicin sulfate, piperacillin-tazobactam (EDTA-free), potassium chloride, remifentanil, sodium bicarbonate, suxamethonium, tobramycin, vancomycin, zidovudine.
Incompatibility	Azithromycin, calcium gluconate, ceftriaxone, ciprofloxacin, cefalothin, ganciclovir, gentamicin, kanamycin, magnesium sulfate, penicillin or carbenicillin, pentamidine, phenobarbital.
Stability	Mylan: To reduce microbiological hazard, use as soon as practicable after dilution. If storage is necessary, hold at 2 to 8°C for not more than 24 hours.[8]
Storage	Dalacin C: Store below 8°C. Do not freeze. Mylan brand: Store below 25°C.

Excipients	Dalacin C: Benzyl alcohol, disodium edetate, hydrochloric acid, sodium hydroxide, water for injections. Mylan brand: Disodium edetate, water for injections, hydrochloric acid and sodium hydroxide. Mylan brand does not contain benzyl alcohol.
Special comments	
Evidence	**Background** Clindamycin is effective in vitro against many gram positive cocci, particularly Group A beta-haemolytic streptococci, *Streptococcus pneumoniae*, and methicillin-susceptible and resistant *Staphylococcus aureus*, though all of these may be resistant to clindamycin and susceptibility should be confirmed. It may also be effective against a wide range of gram positive anaerobic bacteria, including penicillin-resistant Bacteroides species. Aerobic gram negative bacteria are not usually susceptible to clindamycin.[3] It is used as the alternate to penicillin in streptococcal and staphylococcal infections and as a primary agent for infections caused by penicillin resistant anaerobic bacilli.[4] It is approved for adults and children for systemic treatment of staphylococcal, streptococcal, and anaerobic bacterial infections and complicated intraabdominal infections.[1, 5] Because of its profile and high oral bioavailability, it is also suggested as part of an oral multimodal alternative for prolonged parenteral antibiotic regimens e.g. to treat bone and joint or prosthesis-related infections.[1] **Efficacy** Gonzalez et al performed a prospective, multicentre clinical trial to determine pharmacokinetics (PK) and safety of intravenous clindamycin in preterm and term infants.[2] In this study, authors developed population based PK model using the combined PK data collected from 3 prospective clinical trials: Staph Trio, PTN POPS and CLIN01. From Staph Trio trial, authors enrolled 21 infants with median (range) GA and postnatal age (PNA) of 26 weeks (23-29) and 23 days (5 to 65), respectively. The median (range) number of clindamycin samples per infant was 3 (2 to 4). They combined this data with additional PK samples collected from 41 preterm and term infants <121-day postnatal age in PTN POPS trial. The median (range) GA and PNA values from PTN POPS trial were 33 weeks (22-42 weeks) and 16 days (1 to 115) respectively. The median clindamycin dose was 5.1 mg/kg/dose (3.8 to 13.5) and 15 mg /kg/day (7.6 to 40.6). The final population PK model developed by the authors using simulated PMA-based intravenous dosing regimens administered every 8 h (≤32 weeks PMA, 5 mg/kg; 33 to 40 weeks PMA, 7 mg/kg; >40 to 60 weeks PMA, 9 mg/kg) resulted in an unbound, steady-state concentration at half the dosing interval greater than a MIC for S. aureus of 0.12 µg/mL in >90% of infants (targeted similar $AUC_{ss\ 0\text{-}8h}$ across age).[2] There were no adverse events related to clindamycin use in this study. **Pharmacokinetics** Clindamycin undergoes hepatic metabolism to the major bioactive sulfoxide and N-demethyl metabolites. **Safety** Clindamycin is well tolerated and no serious adverse effects attributable to clindamycin were reported. Increased incidence of necrotising enterocolitis (OR 1.95).[1, 2]
Practice points	
References	1. Greenberg RG, Wu H, Maharaj A, Cohen-Wolkowiez M, Tomashek KM, Osborn BL, et al. A Pharmacoepidemiologic Study of the Safety and Effectiveness of Clindamycin in Infants. Pediatric Infectious Disease Journal. 2020;39(3):204-10. 2. Gonzalez D, Delmore P, Bloom BT, Cotten CM, Poindexter BB, McGowan E, et al. Clindamycin Pharmacokinetics and Safety in Preterm and Term Infants. Antimicrob Agents Chemother. 2016;60(5):2888-94. 3. Fass RJ, Ruiz DE, Gardner WG, Rotilie CA. Clindamycin and gentamicin. Archives of Internal Medicine. 1977;137(1):28-38. 4. Derrick CW, Jr., Reilly KM. Erythromycin, lincomycin, and clindamycin. Pediatric Clinics of North America. 1983;30(1):63-9. 5. Solomkin JS, Mazuski JE, Bradley JS, Rodvold KA, Goldstein EJ, Baron EJ, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. Surgical infections. 2010;11(1):79-109.

	6. Meyers RS, Thackray J, Matson KL, McPherson C, Lubsch L, Hellinga RC, Hoff DS. Key Potentially Inappropriate Drugs in Pediatrics: The KIDs List. J Pediatr Pharmacol Ther. 2020;25(3):175-191. doi: 10.5863/1551-6776-25.3.175. 7. Clindamycin. Australian Injectable drugs handbook. 8th edition. Accessed on 8 June 2022. 8. Mylan Clindamycin. Product info. MIMS online. Accessed on 6 June 2022.

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