Cefalexin (Cephalexin) 2019

For newborn use only

Alert	The Antimicrobial Stewardship Team recommends this drug is listed under the following category: Unrestricted.
Indication	Treatment of mild infections due to susceptible strains of bacteria. Prophylaxis of urinary tract infections in patients at risk (e.g. vesicoureteric reflux).
Action	First generation cephalosporin. Bactericidal – inhibits cell wall synthesis in susceptible organisms. Most active against Gram-positive cocci, including MSSA and streptococci. Has have no activity against enterococci, MRSA or *Listeria*.[1]
Drug Type	Cephalosporin antibiotic.
Trade Name	APO-Cephalexin, Cefalexin Sandoz, Ialex, Ibilex, Keflex.
Presentation	125 mg/5 mL suspension 250 mg/5mL suspension
Dosage / Interval	**Treatment** **Method** / **Interval** **Postnatal Age (Days)** / **Dose** 0–7 days: 25 mg/kg: 12-hourly 8–28 days: 25 mg/kg: 8-hourly 29+ days: 25 mg/kg: 6-hourly **Prophylaxis of urinary tract infection (UTI)** 12.5 (10–15) mg/kg/dose DAILY (maximum dose 125 mg daily).[7,8] **Prophylaxis around Voiding Cystourethrogram** 12.5 (10–15) mg/kg/dose 8-hourly for 3 days (day prior, on the day and one day after MCU).[10]
Route	Oral
Maximum Daily Dose	500 mg
Preparation/Dilution	Powder usually reconstituted by Pharmacy. If supplied unreconstituted, reconstitute powder for oral suspension using water for injection with the volume specified on the bottle.
Administration	Oral: Prophylactic dose: May be taken with or without food. Treatment dose: Preferably commence treatment without feeds (faster absorption and higher peak concentrations)[3] Shake bottle well before measuring dose.
Monitoring	Monitor renal, hepatic and haematological function with prolonged use.
Contraindications	Hypersensitivity to cephalosporins. Immediate hypersensitivity or severe reaction to penicillins.
Precautions	Use with caution in patients with hypersensitivity or mild adverse reactions to penicillins or carbapenems as cross-reactivity can occur (e.g. rash).
Drug Interactions	Nil relevant.
Adverse Reactions	Diarrhoea, dyspepsia, abdominal pain, nausea and vomiting. Pseudomembranous colitis (rare). Transient elevation of liver enzymes. Hypersensitivity: Immediate – urticaria, bronchospasm, anaphylaxis. Delayed – maculopapular rash, fever, eosinophilia.
Compatibility	Can be given with food.
Incompatibility	Not applicable.
Stability	Reconstituted solution should be discarded after 14 days.
Storage	Store powder below 25°C Store reconstituted solution between 2 and 8°C
Special Comments	May cause false positive Coombs test. Consider increasing dosing interval in significant renal impairment.

Evidence summary	**Pharmacokinetics and pharmacodynamics** First-generation cephalosporins are most active against gram-positive cocci, including MSSA and streptococci. They have no activity against enterococci, MRSA, or *Listeria*. Therapeutic concentrations occur in most tissues, including pleura, synovial fluids, and bone, but not middle ear fluid. First-generation cephalosporins should not be used if bacterial meningitis is possible, due to poor CSF penetration, with or without inflammation.[1] Cefalexin is rapidly absorbed in the upper intestine. Distribution to the tissues, other than the spinal fluid and aqueous humour, is rapidly achieved. Cefalexin does not penetrate host cells, which probably accounts for its low incidence of side effects. Binding to human serum proteins is low and there is no measurable metabolism in body fluids. Cefalexin is rapidly cleared from the body by the kidneys. In adults, 70 to 100% of the dose is found in the urine 6–8 h after each dose. The elimination half-life was 0.8 hours in adults.[2] In infants and children, following ingestion of a 15 mg/kg dose, mean peak concentrations of cefalexin in serum were achieved at one-half hour (23.4 microgram/mL) in fasting and at one hour (9.0 microg/mL) in non-fasting patients. Administration of drug with milk reduced the mean peak concentration by 60% and the area-under-the-curve value by approximately 40%. The half-life in serum was approximately 60 minutes. Concentrations in tears and saliva were below MIC for many organisms.[3] In 40 newborn infants given 15 mg/kg cefalexin every 8 hours the serum concentrations of cefalexin were lower than the average MIC for many of the Gram-negative organisms encountered in the neonatal period. In a second series, in 30 newborn infants who received 50 mg/kg every 12 hours, adequate serum concentrations were achieved. Urinary excretion of cefalexin in 24 hours ranged from 5 to 66% of the total daily dose suggesting 50 to 60% of the administered dose of cefalexin is absorbed by the newborn infant.[4] Pharmacokinetic data are lacking in preterm infants. **Efficacy** Trials on cefalexin in treating specific infections in neonates are lacking. Beyond the neonatal age group, American Academy of Pediatrics recommends a cefalexin dosage of 50–100 mg/kg/day in 4 divided doses.[5,6] Antimicrobial prophylaxis for UTI: The suggested prophylactic dose of cefalexin ranges from 10–12.5 mg/kg/dose daily.[7,8] Due to concerns about bacterial resistance, it is suggested to use cefalexin or amoxicillin (based on culture and susceptibility results) as second-choice antibiotics for prophylaxis beyond 3 months of age.[8] Antimicrobial prophylaxis for micturating cystourethrogram (MCUG): NICE Guideline 2007 recommends a 3-day antibiotic course with MCUG taking place on the second day.[9] Cefalexin 10–15 mg/kg/dose 8-hourly for 3 days in children aged 2 months to 5 years undergoing MCUG was reported to reduce MCUG-associated UTI in a randomised, controlled trial.[10] (LOE:II) **Safety** Non-pruritic rashes occur in 1% to 2.8% of patients and are not a contraindication to future use. True anaphylactic reactions related to cephalosporins are rare, with an estimated risk of 0.0001% to 0.1%. Cephalosporin-induced anaphylaxis is no greater among penicillin-allergic patients according to newer evidence that established that previous rates of cross-reactivity between penicillins and cephalosporins were overestimated.[1]

References	1. Harrison CJ, Bratcher D. Cephalosporins: a review. Pediatr Rev. 2008;29:264-7. 2. Griffith RS. The pharmacology of cephalexin. Postgrad Med J. 1983;59 Suppl 5:16-27. 3. McCracken GH, Jr., Ginsburg CM, Clahsen JC, Thomas ML. Pharmacologic evaluation of orally administered antibiotics in infants and children: effect of feeding on bioavailability. Pediatrics. 1978;62:738-43. 4. Boothman R, Kerr MM, Marshall MJ, Burland WL. Absorption and excretion of cephalexin by the newborn infant. Arch Dis Child. 1973;48:147-50. 5. Paintsil E. Update on recent guidelines for the management of urinary tract infections in children: the shifting paradigm. Curr Opin Pediatr. 2013;25:88-94. 6. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement Management, Roberts KB. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics. 2011;128:595-610. 7. Baracco R, Mattoo TK. Diagnosis and management of urinary tract infection and vesicoureteral reflux in the neonate. Clin Perinatol. 2014;41:633-42. 8. NICE Guidelines. Urinary tract infections. Antimicrobial prescribing. 31 October 2018. https://www.nice.org.uk/guidance/ng112/chapter/Recommendations#treatment-for-children-and-young-people-under-16-years-with-recurrent-uti. 9. NICE Guidelines. Urinary tract infection in under 16s: diagnosis and management. 22 August 2007. https://www.nice.org.uk/guidance/cg54/chapter/Recommendations#imaging-tests 10. Sinha R, Saha S, Maji B, Tse Y. Antibiotics for performing voiding cystourethrogram: a randomised control trial. Arch Dis Child. 2018;103:230-4.

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Authors Contribution

Original author/s	Chris Wake
Author/s of the current review	Srinivas Bolisetty
Evidence Review - original	David Osborn
Expert review	Brendan McMullan, Sean Kennedy, Anne Durkan
Nursing Review	Eszter Jozsa
Pharmacy Review	Jing Xiao, Michelle Jenkins, Cindy Chen
ANMF Group contributors	Nilkant Phad, Himanshu Popat
Final editing and review of the original	Ian Whyte
Electronic version	Cindy Chen, Ian Callander
Facilitator	Srinivas Bolisetty