Antibiotic Dosing Guideline for Cystic Fibrosis

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Cystic Fibrosis Canada
Fibrose kystique Canada

FURTHER

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This is an antibiotic dosing guideline for cystic fibrosis patients, but individual patient factors must be considered when calculating and choosing a dose. These factors may include, but are not limited to: body weight, renal or hepatic impairment, drug interactions, and history of allergic reactions or intolerances.

The selection of antibiotics (monotherapy or in combination), use of conventional or high dose, and treatment duration are also based on various patient-specific factors such as pathogen(s), antimicrobial sensitivities, and symptom severity, but are not covered in this guideline. Select organisms have been listed for the antimicrobial activity of each antibiotic, and are not representative of the full spectrum of activity of the antibiotic. For information on inhaled antibiotics, please refer to the Canadian Consensus Statement on Aerosolized Antibiotic Use in Cystic Fibrosis, at https://www.cysticfibrosis.ca/about-cf/guidelines-and-standards-of-care.

Antibiotic dosing and therapeutic drug monitoring (TDM) guidance was reviewed by the working group, and is meant to be used alongside local expertise and institution specific practices.

Antibiotic	Antimicrobial activity	Paediatric Dosing and TDM	Adult Dosing and TDM
amikacin	NTM	*Empiric dosing, then adjust based on TDM:* **NTM Induction Phase (3-12 weeks):** <u>Extended interval dosing:</u> - Children: 15-30 mg/kg/dose IV once daily - Adolescents: 10-15 mg/kg/dose IV once daily Max empiric dose: 1500 mg/dose <u>Traditional dosing:</u> - 7.5-10 mg/kg/dose IV q8h Max empiric dose: 500 mg/dose **NTM Maintenance Phase:** - Amikacin parenteral formulation: 250-500 mg nebulized once or twice daily (Amikacin liposome inhalation suspension not routinely used, but available through Health Canada SAP)	*Empiric dosing, then adjust based on TDM:* **NTM Induction Phase (3-12 weeks):** - 10-30 mg/kg/dose IV q24h or - 7.5 mg/kg/dose IV q12h daily to 3x/week **NTM Maintenance Phase:** - Amikacin parenteral formulation: 250-500 mg nebulized once or twice daily (Amikacin liposome inhalation suspension not routinely used, but available through Health Canada SAP) **TDM:** Peak: 20-30 mg/L, Trough: <5-10 mg/L *For treatment of other organisms, please refer to institution specific practices for dosing and TDM targets.* References: 1, 2

		TDM: Extended interval – Peak: 20-30 mg/L, Trough: <5-10 mg/L Traditional – Peak: 20-35 mg/L, Trough: 1-4 mg/L *For treatment of other organisms, please refer to institution specific practices for dosing and TDM targets.* References: 1, 2	
amoxicillin/clavulanic acid	*H. influenzae, S. aureus*	*Dosing based on amoxicillin component:* 30 mg/kg/dose PO TID or 45 mg/kg/dose PO BID Max: 3 g/24 h (using 7:1 formulation and additional amoxicillin) Reference: 2	*Dosing based on amoxicillin component:* 875 mg PO BID (using 7:1 formulation) or 500 mg PO TID (using 4:1 formulation) Reference: 2
azithromycin	NTM	**NTM Treatment:** 10-12 mg/kg/dose PO once daily Max: 500 mg/dose **Anti-inflammatory:** - Less than 25 kg: 10 mg/kg/dose PO daily 3x/week (Mon/Wed/Fri) - 25-40 kg: 250 mg PO daily 3x/week (Mon/Wed/Fri) - 40 kg or greater: 500 mg PO daily 3x/week (Mon/Wed/Fri) References: 1, 3, 4	**NTM Treatment:** 250-500 mg PO once daily **Anti-inflammatory:** 250 mg PO once daily or 500 mg PO daily 3x/week (Mon/Wed/Fri) References: 1, 3, 5
aztreonam	*B. cepacia* complex, *P. aeruginosa*	**Requires Health Canada SAP approval* 37.5-75 mg/kg/dose IV q6h Max:12 g/24 h References: 2, 6	**Requires Health Canada SAP approval* 2 g IV q6h to q8h Max: 12 g/24 h Reference: 6

cefazolin	*S. aureus*	50 mg/kg/dose IV q8h or 37.5 mg/kg/dose IV q6h Max: 2 g/dose References: 2, 7 (extrapolated from osteomyelitis dosing)	2 g IV q8h Reference: 2
cefepime	*B. cepacia* complex, *P. aeruginosa*	50 mg/kg/dose IV q8h May consider 50 mg/kg/dose IV q6h for resistant organisms Max: 2 g/dose References: 2, 8	2 g IV q8h May consider 2 g IV q6h for resistant organisms References: 2, 8
cefotaxime	*H. influenzae*	50-75 mg/kg/dose IV q6h Max: 2 g/dose Reference: 2	1-2 g IV q8h Reference: 2 (adapted from pneumonia dosing)
cefoxitin	NTM	200 mg/kg/day IV divided q6h to q8h Max: 12 g/24 h References: Adapted from 1, 2	200 mg/kg/day IV divided q6h to q8h Max: 12 g/24 h References: 1, 2
cefprozil	*H. influenzae, S. aureus*	15 mg/kg/dose PO BID Max: 500 mg/dose Reference: 2	500 mg PO BID Reference: 2
ceftazidime	*Achromobacter spp.*, *B. cepacia* complex, *P. aeruginosa*	200-400 mg/kg/day IV divided q6h to q8h Max: 12 g/24 h Reference: 8	2-3 g IV q6h to q8h Max: 12 g/24 h References: 2, 8
ceftazidime/avibactam	MDR GNB, *P. aeruginosa*	*Dosing based on ceftazidime component:* - 3-6 months old: 40 mg/kg/dose IV q8h - Greater than 6 months old: 50 mg/kg/dose IV q8h Max: 2 g/dose Reference: 2 (extrapolated dosing)	*Dosing based on ceftazidime/avibactam combination:* 2.5 g IV q8h References: 2, 9

ceftolozane/ tazobactam	MDR GNB	*No paediatric dosing published*	*Dosing based on ceftolozane/tazobactam combination:* 3 g IV q8h References: 10, 11, 12
cefuroxime	*H. influenzae, S. aureus*	**Intravenous:** 50 mg/kg/dose IV q8h Max: 1.5 g/dose **Oral:** 15 mg/kg/dose PO BID Max: 500 mg/dose Reference: 2	**Intravenous:** 1.5 g IV q8h **Oral:** 500 mg PO BID Reference: 2
cephalexin	*S. aureus*	25 mg/kg/dose PO QID Max: 1 g/dose Reference: 2	500 mg to 1 g PO QID Reference: 2
chloramphenicol	*Achromobacter spp.*, *B. cepacia* complex	12.5-25 mg/kg/dose IV q6h Max: 1 g/dose **TDM:** Peak: 15-30 mcg/mL, Trough: 5-15 mcg/mL Reference: 2	12.5-25 mg/kg/dose IV q6h Max: 1 g/dose **TDM:** Peak: 10-20 mcg/mL, Trough: 5-10 mcg/mL Reference: 2
ciprofloxacin	*Achromobacter spp.*, *P. aeruginosa*	**Intravenous:** 10 mg/kg/dose IV q8h Max: 400 mg/dose **Oral:** 20 mg/kg/dose PO BID Max: 1 g/dose Reference: 13	**Intravenous:** 400 mg IV q8h **Oral:** 750 mg PO BID-TID References: 13, 14

cloxacillin	*S. aureus*	**Intravenous:** 50 mg/kg/dose IV q6h Max: 2 g/dose **Oral:** 50 mg/kg/dose PO q6h Max: 1 g/dose References: 2, 15	1-2 g IV q6h Reference: 2
colistin	*Achromobacter spp.*, *P. aeruginosa*	*Dosing expressed in terms of mg of colistin base activity:* 1-1.67 mg/kg/dose IV q8h Max: 100 mg/dose References: 2, 16	*Dosing expressed in terms of mg of colistin base activity:* 2.5-5 mg/kg/day IV divided q8h to q12h Max: 5 mg/kg/24 h References: 2, 16
doxycycline	MRSA	8 years and older: 2 mg/kg/dose PO BID Max: 100 mg/dose Reference: 2	100 mg PO BID References: 2, 17
fosfomycin	MDR organisms	*Use in consultation with Infectious Diseases Specialist* - 1 to 12 months (up to 10 kg) 200-300* mg/kg/day IV divided q8h - 1 to 12 years (10 to 40 kg) 200-400* mg/kg/day IV divided q6h to q8h Max: 8 g/dose, 16 g/24 h - 12 years and older (greater than 40 kg) 12-24* g/day IV divided q6h to q12h Max: 8 g/dose, 16 g/24 h *doses above 300 mg/kg/day or 16 g/day may be considered for severe and serious infections Reference: 18	*Use in consultation with Infectious Diseases Specialist* 12-24* g/day IV divided q6h to q12h Max: 8 g/dose, 16 g/24 h *doses above 16 g/day may be considered for severe and serious infections Reference: 18

imipenem/cilastatin	*Achromobacter spp.,* NTM, *P. aeruginosa*	*Dosing based on imipenem component:* **Pulmonary Exacerbations:** 25 mg/kg/dose IV q6h Max: 1 g/dose **NTM Treatment:** 15-20 mg/kg/dose IV q12h Max: 1 g/dose References: 1, 6	*Dosing based on imipenem component:* **Pulmonary Exacerbations:** 1 g IV q6h **NTM Treatment:** 1 g IV q12h References: 1, 2, 6
levofloxacin	*Achromobacter spp., B. cepacia* complex, *S. maltophilia*	- 6 months to 5 years: 10 mg/kg/dose PO/IV q12h Max: 750 mg/24 h - 5 years and older: 10 mg/kg/dose PO/IV once daily Max: 750 mg/dose Reference: 2	750 mg PO/IV once daily References: 2, 19
linezolid	MRSA, NTM	**Pulmonary Exacerbations:** - Less than 12 years old: 10 mg/kg/dose PO/IV q8h Max: 600 mg/dose - 12 years and older: 10 mg/kg/dose PO/IV q12h Max: 600 mg/dose **NTM Treatment:** - Less than 12 years old: 10 mg/kg/dose PO/IV q8h Max: 600 mg/dose - 12 years and older: 10mg/kg/dose PO/IV q12h to q24h* Max: 600 mg/dose *May reduce to once daily if intolerant to adverse effects References: 1, 2	**Pulmonary Exacerbations:** 600 mg PO/IV q12h **NTM Treatment:** 600 mg PO/IV q12h to q24h* *May reduce to once daily if intolerant to adverse effects References: 1, 2

meropenem	*Achromobacter spp., B. cepacia* complex, *P. aeruginosa*	40 mg/kg/dose IV q8h Max: 2 g/dose Reference: 6	2 g IV q8h References: 2, 6
minocycline	*Achromobacter spp., B. cepacia* complex, *S. maltophilia*	Older than 8 years: 4 mg/kg PO once as loading dose (Max: 200 mg/dose), then 2 mg/kg/dose PO BID (Max: 100 mg/dose) Reference: 2	100 mg PO BID Reference: 2
moxifloxacin	*Achromobacter spp.,* NTM, *S. maltophilia*	- Less than 15 years: 10 mg/kg/dose PO/IV once daily Max: 400 mg/dose - 15 years and older: 400 mg PO/IV once daily References: 1, 2	400 mg PO once daily References: 1, 2
piperacillin/ tazobactam	*Achromobacter spp., P. aeruginosa*	*Dosing based on piperacillin component:* 350-600 mg/kg/day IV divided q4h to q6h Max: 4 g/dose References: 2, 8	*Dosing based on piperacillin/tazobactam combination:* 4.5 g IV q4h to q6h References: 2, 8
sulfamethoxazole (SMX)/trimethoprim (TMP)	*Achromobacter spp., B. cepacia* complex, MRSA, *S. maltophilia*	*Dosing based on TMP component:* Mild infection: 6 mg/kg/dose PO BID PO Max: 320 mg/dose Moderate to severe infection: 5 mg/kg/dose PO/IV q6h to q8h PO Max: 320 mg/dose Reference: 2	*Dosing based on TMP component:* Mild infection: 320 mg PO BID Moderate to severe infection: 5 mg/kg/dose IV q6h to q8h Reference: 2

temocillin	*B. cepacia* complex	*No paediatric dosing published*	**Requires Health Canada SAP approval* *Dosing based on temocillin base:* 2 g IV q12h Severe infection: 2 g IV q8h Reference: 20
tigecycline	*Achromobacter spp.,* MRSA, NTM, *S. maltophilia*	**Pulmonary Exacerbations:** - 8-11 years: 1.2-2 mg/kg/dose IV q12h Max: 50 mg/dose - 12 years and older: 50 mg IV q12h **NTM Treatment:** - 8-11 years: 1.2 mg/kg/dose IV q12h Max: 50 mg/dose - 12 years and older: 100 mg IV once as loading dose, then 50 mg IV q12h to q24h References: 1, 2	**Pulmonary Exacerbations:** 100 mg IV once as loading dose, then 50 mg IV q12h *****The loading and maintenance doses may need to be doubled in treatment of more drug-resistant bacteria and/or severe infection **NTM Treatment:** 100 mg IV once as loading dose, then 50 mg IV q12h to q24h References: 1, 21, 22
tobramycin	*P. aeruginosa*	*Empiric dosing, then adjust based on TDM:* <u>Extended interval dosing:</u> 10 mg/kg/dose IV q24h <u>Traditional dosing:</u> 4 mg/kg/dose IV q8h **TDM:** Extended interval – Peak: 20-40 mg/L, Trough: <1 mg/L Traditional – Peak: 10-12 mg/L, Trough: <2 mg/L References: 2, 23, 24	*Empiric dosing, then adjust based on TDM:* <u>Extended interval dosing:</u> 10 mg/kg/dose IV q24h **TDM:** Peak: 20-40 mg/L, Trough: <1 mg/L References: 2, 23, 24

vancomycin	MRSA	*Empiric dosing, then adjust based on TDM:* 15 mg/kg/dose IV q6h **TDM:** - Trough: 10-20 mg/L - AUC/MIC ratio: 400-600 References: 2, 25	*Empiric dosing, then adjust based on TDM:* <u>Intermittent Infusion:</u> 15-20 mg/kg/dose IV q8h to q12h (rounded to the nearest 250 mg) *Loading dose may be considered in seriously ill patients <u>Continuous Infusion:</u> 15-20 mg/kg IV once as loading dose, then 30-40 mg/kg/day (up to 60 mg/kg/day) IV as maintenance continuous infusion **TDM:** - Trough: 15-20 mg/L - AUC/MIC ratio: 400-600 - Continuous infusion: Steady-state concentration of 20-25 mg/L References: 2, 17, 25

AUC, area under the curve; **BID**, twice daily; **MDR GNB**, multidrug-resistant Gram negative bacilli; **MIC**, minimum inhibitory concentration; **MRSA**, methicillin-resistant *Staphylococcus aureus*; **NTM**, nontuberculous mycobacteria including *Mycobacterium abscessus complex* and *Mycobacterium avium complex*; **QID**, four times daily; **SAP**, Special Access Programme; **TDM**, therapeutic drug monitoring; **TID**, three times daily

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