Guideline

Empirical antimicrobial therapy for children with Cystic Fibrosis

Document ID	CHQ-GDL-01073	Version no.	4.0	Approval date	25/08/2023	
Executive sponsor	Executive Director of Medical Se	Executive Director of Medical Services			01/09/2023	
Author/custodian Director Respiratory Medicine				Review date	25/08/2025	
Author/custodian	Director Infection Management and Prevention Service, Immunology and Rheumatology					
Supersedes	3.0					
Applicable to	All Children's Health Queensland staff caring for patients with Cystic Fibrosis					
Authorisation	Executive Director Clinical Services					

Purpose

This guideline provides Children's Health Queensland (CHQ) recommendations for empirical antimicrobial therapy for children with Cystic Fibrosis (CF), for inpatient and outpatient management.

Scope

This guideline provides information for CHQ staff caring for paediatric CF patients.

Related documents

Procedures, Guidelines, Protocols

- CHQ Paediatric Medication Guideline IV Aminoglycosides
- CHQ Paediatric Medication Guideline Vancomycin
- CHQ@Home Outpatient Parenteral Antimicrobial Therapy Prescribing, Administration and monitoring guideline
- <u>CHQ-PROC-01036 Antimicrobial: Prescribing, Management and Stewardship</u> and <u>CHQ Antimicrobial</u> Restriction list
- CHQ-PROC-63223 Management of patients with cystic fibrosis
- CHQ-GDL-01061 Immunisation Guideline for Medically at Risk Children
- CHQ-GDL-01076 Paediatric antibiotic allergy assessment, testing and de-labelling
- <u>CHQ-GDL-70047 Clinical guidelines for the care of children and adolescents with Cystic Fibrosis Volume 1: Respiratory Care</u>



Guideline

Empirical antimicrobial therapy for patients with Cystic Fibrosis

Part 1. Summary table of empirical antimicrobial therapy for children with Cystic Fibrosis (CF)

- Pulmonary Exacerbation Pseudomonas aeruginosa (PsA) negative
- Pulmonary Exacerbation PsA eradication
- Chronic PsA colonisation exacerbation
- Chronic PsA colonisation maintenance therapy
- Methicillin Resistant Staphylococcus Aureus (MRSA) eradication outpatient treatment
- MRSA Pulmonary optimisation inpatient treatment
- Burkholderia cepacia complex eradication inpatient treatment
- Non-tuberculous mycobacterium (NTM) induction and maintenance treatment (Quick reference guide)

Part 2. Hospital In The Home (HITH)

Part 3. Non-tuberculous mycobacterium (NTM) eradication – induction and maintenance treatment

Part 4. Fungal infections

Allergic bronchopulmonary aspergillosis (ABPA)

Part 5. Summary table of antibiotic doses recommended in Cystic Fibrosis (CF)

- Additional monitoring whilst on intravenous (IV) antibiotics
- Intravenous antibiotics
- Oral antibiotics
- Inhaled or nebulised antibiotics



Part 1. Summary table of empirical antimicrobial therapy for children with Cystic Fibrosis

For patients with a history of immediate or delayed type penicillin and/or cephalosporin hypersensitivity, please consult the Infectious Diseases team (ID) for advice on treatment options prior to commencement of antibiotics. For patients enrolled in BEAT CF trial, empirical antimicrobials will be tailored to randomisation with Infectious diseases approval according to AMS Formulary.

Clinical Scenario		Antibiotic	Duration	Alternative antibiotic	Comments
Cystic Fibrosis Exacerbation Pseudomonas aeruginosa (PsA) negative	Inpatient or HITH	Piperacillin/Tazobactam IV 100 mg/kg/dose 6-hourly (maximum 4 g Piperacillin component/dose) PLUS Tobramycin IV* Dosing: Refer to CHQ-PMG-01294 Intravenous Aminoglycoside therapy (Amikacin, Gentamicin and Tobramycin) (or previously optimised dose from a recent admission (within last three months), speak to a Pharmacist for advice)	14 days	Ceftazidime (plus IV Tobramycin) is an alternative if no S.aureus isolated Ceftazidime IV 100 mg/kg/dose 8-hourly (maximum 4 g/dose) If ceftazidime used and S.aureus present, add in Flucloxacillin: Flucloxacillin IV 50 mg/kg/dose 6-hourly (maximum 2 g/dose) or Oral Flucloxacillin 25 mg/kg/dose four times daily (maximum 1 g/dose)	Monitoring: Baseline and then weekly Full blood count (FBC) & Electrolytes and liver function tests (eLFTS or CHEM20), vestibular toxicity monitoring whilst on IV Tobramycin *See Part 5 for IV Tobramycin therapeutic drug monitoring (TDM) Pre-approved HITH: IV Tobramycin (once daily) and IV Piperacillin/ Tazobactam (continuous infusion via ambulatory device) or Ceftazidime (via intermate device) for 14 days.
Cystic Fibrosis Exacerbation Pseudomonas aeruginosa (PsA) negative	Outpatient	Amoxycillin-clavulanic acid (DUO preparation) 25 mg/kg/dose orally 12-hourly (maximum 875 mg Amoxycillin component/dose)	14 days to 6 weeks	Trimethoprim/Sulfamethoxazole Oral 4 mg/kg/dose twice daily (maximum 160 mg/dose Trimethoprim component)	Monitoring: FBC and CHEM20 once a month whilst on high dose Trimethoprim/Sulfamethoxazole



Clinical Scenario		Antibiotic	Duration	Alternative antibiotic	Comments
Cystic Fibrosis – Pseudomonas aeruginosa (PsA) Eradication	Inpatient or HITH	Piperacillin/Tazobactam IV 100 mg/kg/dose 6-hourly (maximum 4 g Piperacillin component/dose) PLUS Tobramycin IV* Dosing: Refer to CHQ-PMG-01294 Intravenous Aminoglycoside therapy (Amikacin, Gentamicin and Tobramycin) (or previously optimised dose from a recent admission (within last 3 months), speak to a Pharmacist for advice) Followed by Tobramycin inhaled: 0 to 18 years: 300 mg nebulised 12 hourly	14 days	Ceftazidime (plus IV Tobramycin) an alternative if no S.aureus isolated Ceftazidime IV 100 mg/kg/dose 8-hourly (max 4 g/dose) If Ceftazidime used and S.aureus present, add in Flucloxacillin: Flucloxacillin IV 50 mg/kg/dose 6-hourly (max 2 g/dose) or Oral Flucloxacillin 25 mg/kg/dose four times daily (max 1 g/dose)	Monitoring: Baseline and then weekly FBC & CHEM20, vestibular toxicity monitoring whilst on IV Tobramycin *See Part 5 for IV Tobramycin TDM Pre-approved HITH: IV Tobramycin (once daily) and IV Piperacillin/ Tazobactam (continuous infusion via ambulatory device) or Ceftazidime (via intermate device) for 14 days.
Cystic Fibrosis – Pseudomonas aeruginosa (PsA) Eradication	Outpatient	Tobramycin inhaled (use preservative free formulation) 0 to 18 years: 300 mg 12-hourly If treatment failure or Tobramycin resistant: Oral Ciprofloxacin 20 mg/kg/dose orally 12-hourly (maximum 1 g/dose) PLUS Inhaled Colistin (Tadim®) 1 to 2 years: 1 million units inhaled 12-hourly 2 to 18 years: 2 million units inhaled 12-hourly	4 weeks 4 weeks 12 weeks		Eradication should be attempted for all children on first/new isolation of <i>Pseudomonas aeruginosa</i> Consider the impact of type of nebuliser when choosing Colistin dose see Part 5 (29) Prescription for Sodium Chloride 0.9% ampoules also required when prescribing Inhaled Colistin (required for reconstitution).



Clinical Scenar	io	Antibiotic	Duration	Alternative antibiotic	Comments
Cystic Fibrosis Exacerbation Chronic Pseudomonas aeruginosa colonisation	Inpatient or HITH	Piperacillin/tazobactam IV 100 mg/kg/dose 6-hourly (maximum 4 g Piperacillin component/dose) PLUS Tobramycin IV* Dosing: Refer to CHQ-PMG-01294 Intravenous Aminoglycoside therapy (Amikacin, Gentamicin and Tobramycin) (or previously optimised dose from a recent admission (within last 3 months), speak to a Pharmacist for advice)	14 days	Ceftazidime (plus IV Tobramycin) an alternative if no S.aureus isolated. Ceftazidime IV 100 mg/kg/dose 8-hourly (maximum 4 g/dose) If Ceftazidime used and S.aureus present, add in Flucloxacillin: Flucloxacillin IV 50 mg/kg/dose 6-hourly (maximum 2 g/dose) OR Oral Flucloxacillin 25 mg/kg/dose four times daily (maximum 1 g/dose)	Monitoring: Baseline and then weekly FBC & CHEM20, vestibular toxicity monitoring whilst on IV Tobramycin. *See Part 5 for IV tobramycin TDM Pre-approved HITH: IV Tobramycin (once daily) and IV Piperacillin/ Tazobactam (continuous infusion via ambulatory device) or Ceftazidime (via intermate device) for 14 days.
Cystic Fibrosis Exacerbation – Chronic Pseudomonas aeruginosa colonisation	Outpatient	Tobramycin inhaled (use preservative free formulation): 0 to 18 years: 300 mg nebulised 12-hourly or More than 6 years old: TOBI® podhaler 112 mg (4 caps) 12-hourly	4 weeks	If on cyclical inhaled Tobramycin may consider adding oral Ciprofloxacin 20 mg/kg/dose twice daily (maximum 1 g/dose) for two weeks.	
Cystic Fibrosis – Chronic Pseudomonas aeruginosa Maintenance therapy	Outpatient	Alternate month Tobramycin inhaled (use preservative free formulation): 0 to 18 years: 300 mg nebulised 12-hourly Or More than 6 years: TOBI® podhaler 112 mg (4 caps) 12-hourly	Long term	If resistant organism or intolerant of TOBI® consider alternate month inhaled Colistin plus Oral Ciprofloxacin (2 to 4 weeks). If deterioration consistently in the month off inhaled antibiotics or frequent exacerbations (three or more/ year) consider continuous alternating inhaled therapy (CAIT) using inhaled Tobramycin alternating with inhaled Colistin plus oral Ciprofloxacin for two of the four weeks.	Consider the impact of type of nebuliser when choosing Colistin dose see Part 5 (29) Prescription for Sodium Chloride 0.9% ampoules also required when prescribing Inhaled Colistin (required for reconstitution)



Clinical Scenario		Antibiotic	Duration	Alternative antibiotic	Comments
Methicillin Resistant Staphylococcus Aureus (MRSA) Eradication	Outpatient	Oral Rifampicin 15 mg/kg/dose once daily (maximum 600 mg/dose) (see note) PLUS, either Oral Trimethoprim/Sulfamethoxazole 8 mg/kg/dose twice daily (max 320 mg/dose trimethoprim component) or Oral Sodium Fusidate 12 mg/kg/dose orally 8-hourly (max 500 mg/dose) (Sodium Fusidate 250 mg tablets are available in Australia) Fusidic acid oral suspension is not TGA registered and only available via the Special Access Scheme (SAS). The suspension is not bioequivalent to Sodium Fusidate tablets. Fusidic Acid oral suspension15 mg/kg/dose orally 8-hourly (maximum 750 mg/dose) Use in conjunction with CHQ-GDL-01063 Recurrent Boils (furunculosis): Guidelines for management and Staphylococcal decolonisation (MRSA and MSSA). This includes Triclosan 1% body washes and Nasal Mupirocin 2% (Bactroban®) for at least 5 days and enhanced household cleaning. Repeat course if respiratory sample MRSA positive at end of 14 days or incomplete clinical improvement or Admit for IV therapy if MRSA positive at end of 14 days and clinical requirement for pulmonary optimisation	14 days	Check MRSA antibiotic susceptibilities prior to treatment and discuss with ID Rifampicin can interact with numerous medications. Pharmacy review prior to commencement. Do not use Rifampicin if on Ivacaftor or Lumacaftor or Tezacaftor or Elxacaftor. Consider washout periods when starting/stopping therapy. If unable to use Rifampicin substitute with oral Clindamycin 10 mg/kg/dose three times daily (maximum 600 mg/dose) (maximum 40 mg/kg/day; maximum 1.8 g/day) Oral Clindamycin has poor palatability, consider rounding doses to the nearest 150mg if appropriate to reduce need to obtain part doses from capsules. For children unable to swallow capsules whole, monitor compliance closely. Sodium Fusidate/Fusidic acid: Food delays absorption. Give on an empty stomach if possible. Alternative method to reduce gastrointestinal side effects: give with or soon after food.	Isolation of MRSA: MRSA on BAL or induced/lower respiratory sample on one sample or MRSA on upper respiratory sample (e.g. cough swab) on two samples more than one week apart. Consider MRSA Eradication therapy: At first isolation of MRSA, or if previously cleared of MRSA, aim for eradication. Upon completion of two weeks of oral antibiotics: Repeat respiratory sample MRSA negative: repeat testing as clinically indicated (usually three monthly) Monitoring: Baseline and then 2 to 4 weekly FBC & CHEM20



Clinical Scenario		Antibiotic	Duration	Alternative antibiotic	Comments
MRSA Pulmonary Optimisation	Inpatient	Admission for IV antibiotics that target MRSA only Lincomycin IV 15 mg/kg/dose 6-hourly (maximum 1.2 g/dose) PLUS Rifampicin PO 15 mg/kg/dose once daily (maximum 600 mg once daily) (see note*) PLUS Inhaled Tobramycin (use preservative free formulation) 0 to 18 years: 300 mg nebulised 12 hourly Followed by: 2 weeks of dual oral eradication therapy	14 days	Check MRSA antibiotic susceptibilities prior to treatment and discuss with ID Do not use if also targeting other pathogens. Discuss with ID. Note*: Rifampicin can interact with numerous medications. Pharmacy review prior to commencement. Do not use Rifampicin if on Ivacaftor or Lumacaftor or Tezacaftor or Elexacaftor. Consider washout periods when starting/stopping therapy.	Eradication of MRSA achieved when: More than 3 months has elapsed since the last positive sample No exposure to antibiotics or antiseptic body washes for the two weeks prior to screening Two negative samples from the site that have previously been MRSA positive, taken one week apart Monitoring: Baseline and then 2 to 4 weekly FBC & CHEM20
				If Lincomycin resistant: Teicoplanin IV 10 mg/kg/dose 12-hourly (maximum 800 mg/dose) for 3 doses (Loading dose), then 10 mg/kg IV once daily (maximum 800 mg/day).	



Clinical Scenario		Antibiotic	Duration	Alternative antibiotic	Comments
Clinical Scenario Burkholderia cepacia complex Eradication	Inpatient	With ID advice and approval only Trimethoprim/Sulfamethoxazole IV 5 mg/kg/dose 8-hourly (max 160 mg/dose Trimethoprim component) PLUS Meropenem IV 40 mg/kg/dose 8-hourly (maximum 2 g/dose) or Ceftazidime IV 100 mg/kg/dose 8-hourly (maximum 4 g/dose) PLUS Tobramycin IV* Dosing: Refer to CHQ-PMG-01294 Intravenous Aminoglycoside therapy (Amikacin, Gentamicin and Tobramycin)	Duration 14 to 21 days	Alternative antibiotic May still use Trimethoprim / Sulfamethoxazole even if B. cepacia shows in-vitro resistance Check antibiotic susceptibilities prior to commencement and discuss with ID	B. multivorans and B. cenocepacia (Bcc) most common. Success rate of eradication therapy is reportedly less than 50% Follow on oral and/or inhaled antibiotic therapy post eradication should be discussed with ID prior to discharge Monitoring: Baseline and then weekly FBC & CHEM20, vestibular toxicity monitoring whilst on IV Tobramycin. *See Part 5 for IV Tobramycin TDM # Trimethoprim/ Sulfamethoxazole IV 5 mg/kg/dose 8-hourly (maximum 160 mg/dose Trimethoprim component) for 48 hours. If renal function remains stable and urine pH > 5.5, consider optimizing to dose to 5 mg/kg/dose 6-hourly (maximum 160 mg/dose
					Trimethoprim component). Monitor renal function and hydration status closely. Risk for renal toxicity and crystalluria.



Clinical Scenar	io	Antibiotic	Duration	Alternative antibiotic	Comments
Mycobacterium abscessus (MABSC) Eradication	Intensive Inpatient	With ID advice and approval only Oral Azithromycin Amikacin* IV Imipenem IV or Cefoxitin IV if macrolide resistant (constitutive or inducible) PLUS Tigecycline IV (> 8 years old)	3 to 4 weeks	With ID advice and approval only Adjust as per sensitivities If macrolide resistant (constitutive or inducible) and <8 years old, consider Clofazimine in induction.	*See Table 1 (Part 3) for amikacin TDM Refer to Table 1 (Part 3) for dosing and monitoring
	Consolidation Outpatient	Amikacin Inhaled (DBL brand is suitable for inhaled use) Oral Clofazimine Oral Azithromycin	12 to 18 months	With ID advice and approval only Oral Moxifloxacin may also be considered	Refer to Table 2 (Part 3) for dosing and monitoring



Part 2. Hospital In The Home (HITH)

- Contact the CHQ@Home Pharmacist / AMS Pharmacist for advice on drug stability and suitable administration device/method. For more information, please refer to <u>Table 1 - Suitability of parenteral</u> <u>antimicrobials for HITH use in paediatrics</u> on the HITH section of the CHQ Antimicrobial Stewardship website.
- For more information on paediatric dosing, administration and monitoring of HITH antimicrobial therapy, refer to: CHQ@Home Outpatient Parenteral Antimicrobial Therapy Prescribing, Administration and monitoring guideline (available via CHQ AMS website).
- The following pre-approved HITH antimicrobial options are available for patients with Cystic Fibrosis:
 - IV Tobramycin (once daily) and IV Piperacillin/Tazobactam (as continuous infusion via ambulatory device) for up to 14 day course. ID approval is required for more than 14 days of treatment.
 - o IV Tobramycin (once daily) and IV Ceftazidime (as 8-hourly dosing each dose administered over 30 minutes via Intermate® ambulatory device. Doses administered by parent/carer after successful completion of CHQ competency training package "Guide to giving your child's IV antibiotic at home for children with PICC lines") for up to 14 day course. ID approval is required for more than 14 days of treatment.
 - All other home parenteral antimicrobial therapy requires ID approval prior to making (HITH) referral.
 Written confirmation of ID approval needs to accompany CHQ@Home (HITH) referral form and/or electronic medical record (ieMR).

Part 3. Mycobacterium abscessus (MABSC) eradication

Non-tuberculous mycobacteria (NTM) are universal environmental organisms that can cause chronic pulmonary infection, particularly in individuals with pre-existing inflammatory lung disease such as CF. Pulmonary disease caused by NTM, particularly MABSC, has emerged as a major threat to the health of individuals with CF but remains difficult to diagnose and problematic to treat (27). The clinical significance of *M.avium* (MAC) or other NTM isolates in children with CF are even less certain than MABSC and rarely require antibiotic treatment.



ALERT

Macrolide monotherapy should be stopped on first identification of NTM in child with CF.

Diagnosis requires a combination of clinical and microbiological criteria (Algorithm 1).

Clinical criteria for diagnosis of NTM (28):

- 1. Pulmonary symptoms, nodular or cavitary opacities on chest radiograph, or a high-resolution computed tomography scan that shows multifocal bronchiectasis with multiple small nodules.
- 2. Appropriate exclusion of other diagnoses.



Microbiologic criteria:

1. Positive culture results from at least two separate sputum samples.

or

2. Positive culture result from at least one bronchial wash or lavage.

Of

3. Transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or acid fast bacilli (AFB)) and positive culture for NTM.

Making the diagnosis of NTM lung disease does not, per se, necessitate the initiation of therapy. Decision to initiate and timing of treatment is based on potential risks and benefits of treatment for the individual patient in discussion with respiratory and ID consultants. For patients enrolled in FoRMAT trial, empirical antimicrobials will be tailored to randomisation with Infectious diseases approval according to AMS Formulary.

MABSC eradication - intensive and consolidation treatment

There are no drug regimens of proven or predictable efficacy for treating MABSC. Guidelines are based on expert opinion and in practice treatments vary considerably. Suggested regimens include an *intensive phase* of 3 to 12 weeks of IV antibiotics (usually Amikacin, Cefoxitin or Imipenem/Cilastatin ± Tigecycline) plus an oral macrolide, with duration based on clinical and microbiological response. This is followed by a *consolidation* phase, that includes oral drugs (usually a macrolide, plus others based on antibiograms, tolerability and experience) and an inhaled IV formulation of Amikacin, for 3 to more than 12 months.

MABSC treatment

Antibiotic plan is dependent on MABSC sensitivities. Sensitivity results must be available prior to elective admission for IV antibiotics for MABSC treatment. Individual treatment plans will be provided by ID.

Suggested intensive phase (inpatient): 3 - 4 weeks

- Oral Azithromycin, Amikacin* IV, Imipenem/Cilastatin IV or Cefoxitin IV
- +/- Tigecycline IV** (More than 8 years old) or oral Clofazimine (Less than 8 years old)
 - o May be added if macrolide resistant (constitutive or inducible) or if clinically otherwise indicated.
- **Tigecycline: May be considered in patients younger than 8 years where benefits outweigh risks after ID and respiratory consultant discussion, and parent consultation.
- Refer to <u>Table 1</u> for dosing recommendations.

Consolidation phase (outpatient): 12 to 18 months

- Oral Azithromycin, oral Clofazimine, Amikacin inhaled (DBL brand is suitable for inhaled use)
- Oral Moxifloxacin **or** oral Linezolid may be additionally considered.
- Refer to <u>Table 2</u> for dosing recommendations.



MAC treatment: 6 to 12 months

Individual treatment plans will be provided by ID.

Usually all oral regime, however if severe disease and high mycobacterial load **Amikacin IV** may be added for up to 4 weeks initially.

- Oral Azithromycin 10 mg/kg once daily (maximum 500 mg/day).
- Oral Rifampicin 10 to 20 mg/kg once daily (maximum 450 mg if less than 40kg, maximum 600 mg if more than 40 kg).
 - o Rifampicin can interact with numerous medications. Pharmacy review prior to commencement. Do not use Rifampicin if on Ivacaftor or Lumacaftor. Seek ID advice for alternatives.
- Oral Ethambutol 15 mg/kg once daily (maximum 1200 mg/day, dose based on lean body weight).
 - Patients taking ethambutol for greater than 2 months could be at risk of optic neuritis. Toxicity is dose and duration dependant, however incidence between adults and children vary (less toxicity observed in children) incidence reported includes: [15mg/kg/day <1%], [25mg/kg/day 5-6%] [>35mg/kg/day 18%]
- Oral Clofazimine may be considered 1 to 5 mg/kg orally once daily (maximum 100 mg/day)
 - Clofazimine is a moderate inhibitor of CYP3A4 and 3A5 isoenzymes. Pharmacy review prior to commencement. Seek ID advice on Clofazimine TDM.

Pre-treatment screening:

- Baseline audiology
- Baseline ECG and repeat at 2 weeks after commencement of treatment (to check for QT prolongation).
- Baseline ophthalmology (within 2 months of commencement of treatment), followed by:
 - 3 monthly ophthalmology review if any of the following risk factors: High dose ethambutol 25mg/kg/day or higher; concurrent hypertension, renal impairment, diabetes, or pre-existing/ concurrent optic nerve co-morbidities
 - If none of the abovementioned risk factors, repeat ophthalmology review at 12 months
- · Baseline CHEM20 and FBC.
- Baseline lactate. Repeat weekly when on Linezolid (high risk of lactic acidosis).
- Please review all the patient's medications and supplements for potential <u>medication interactions</u> with the Clinical Pharmacist before commencement of eradication therapy.



Algorithm 1. Investigation of NTM pulmonary disease in patients with CF

Clinical and radiological suspicion of NTM pulmonary disease

Cease antibiotics active against NTM

(macrolides, trimethoprim/sulfamethoxazole, aminoglycosides, fluroquinolones, tetracycline)

Send three sputum samples for AFB smear and culture

All samples negative for NTM

One sample positive for NTM

Two or more samples positive for the same NTM species

Consider alternative diagnoses

Bronchoscopic aspirate/lavage

NTM pulmonary disease & consider treatment

Sample positive for NTM

NTM pulmonary disease & consider treatment



Table 1. NTM Intensive phase (3-4 weeks – inpatient treatment)

Use a three or four drug combination based on sensitivities and Infectious diseases team advice. For patients enrolled in FoRMAT trial, empirical antimicrobials will be tailored to randomisation with Infectious diseases approval according to AMS Formulary.

Drug	Recommended starting doses	Monitoring
	for infants, children and adolescents with CF	
Amikacin IV	Refer to CHQ-PMG-01294 Intravenous Am Tobramycin)	noglycoside therapy (Amikacin, Gentamicin and
Tigecycline IV (> 8 years of age)	Day 1: (50% of optimal dose) 0.6 mg/kg IV 12-hourly	Please chart Ondansetron to be given 15 to 30 minutes before each tigecycline dose.
	Day 2: (75% of optimal dose) 0.6 mg/kg IV in the morning (max 50mg/dose) and 1.2 mg/kg IV at night (max 50mg/dose)	High incidence of nausea/vomiting – Tigecycline dose titration trialled in other patients with good effect. Second and third line anti-emetics may be required in some patients.
	Day 3: (100% of optimal dose) 1.2 mg/kg IV 12-hourly (maximum 50 mg/dose, maximum 100 mg/day). If tolerated, continue this dose.	Aprepitant (substance P/neurokinin-1 receptor antagonist) may offer some benefits as adjunct antiemetic for patients on NTM treatment. Check drug interactions carefully (Aprepitant is metabolised by CYP3A4). IPA required (non LAM indication)
Imipenem / Cilastatin IV	Day 1 to 2 (75% of optimal dose) 25 mg/kg/dose IV 8-hourly (maximum 1g Imipenem component per dose)	Infuse each dose over 1 to 3 hours to reduce incidence of nausea/vomiting. Note: CF PKPD differences necessitate using higher mg/kg doses.
	Day 3 (100% of optimal dose) 25 mg/kg/dose IV 6-hourly (maximum 1 g imipenem component per dose) (maximum 4 g imipenem component per 24 hours)	Suggest giving regular anti-emetics 15 to 30 minutes before each Imipenem/Cilastatin dose. Additional anti-emetics may be required. Assess on an individual patient basis. Monitor CHEM20 and FBC weekly.
Cefoxitin IV	40 mg/kg/dose IV 6-hourly (maximum 2 g/dose)	Infuse each dose over 3 hours to optimize Time>MIC.
Oral Clarithromycin	7.5 mg/kg/dose orally twice daily (maximum 500 mg/dose)	Check inducible resistance test results before commencing treatment. Risk of QT prolongation. Baseline ECG and repeat at 2 weeks after commencement of treatment. Strong CYP3A4 inhibitor - treatment modifications may be required Please review all the patient's medications and supplements for potential medication interactions with the Clinical Pharmacist before commencement of eradication therapy. Monitor CHEM20.
Oral Azithromycin	10 mg/kg (max 500 mg/day) orally once daily	Risk of QT prolongation. Baseline ECG and repeat at 2 weeks after commencement of treatment. Monitor CHEM20



Table 2. NTM maintenance phase (12 months - outpatient treatment)

Use nebulised Amikacin plus two oral medications based on sensitivities and Infectious diseases team advice. For patients enrolled in FoRMAT trial, empirical antimicrobials will be tailored to randomisation with Infectious diseases approval according to AMS Formulary.

Drug	Recommended starting doses for infants, children and adolescents with CF	Monitoring
Inhaled Amikacin (DBL brand is suitable for inhaled used)	More than 6 years: Inhale 500 mg twice daily **Use after physiotherapy**	Monitor for bronchospasm. Consider using Salbutamol MDI pre-inhaled antibiotics as bronchodilator. Prescription for Sodium Chloride 0.9% ampoules also required when prescribing inhaled Amikacin (required for dilution). The Amikacin DBL 500mg/2mL injectable
		preparation is given via the nebulised route, using a suitable nebuliser with filter attachment (e.g. Pari LC Plus with filter attachment).
Oral Clofazimine	1 mg/kg to 5 mg/kg orally once daily (maximum 100 mg/day)	Risk of QT prolongation. Baseline ECG and repeat at 2 weeks after commencement of treatment. Presumed moderate inhibitor of CyP3A4 and 3A5
	Please note: Children: Limited data, WHO recommendations for MDR-TB and XDR-TB are based on experience and expert	isoenzymes– check drug interactions with clinical pharmacist before commencement of treatment. Monitor CHEM20
	opinion, and suggest 3 to 5 mg/kg/day (max 100 mg/day) (28)	Only available as 50mg and 100mg capsules. Only available through TGA Special Access Scheme Program – additional approvals required
Oral Moxifloxacin	10 mg/kg orally once daily (maximum 400 mg/day)	Risk of QT prolongation. Baseline ECG and repeat at 2 weeks after commencement of treatment. Monitor CHEM20
Oral Clarithromycin	7.5 mg/kg/dose orally twice daily (maximum 500 mg/dose)	Check inducible resistance test results before commencing treatment
	(maximum 500 mg/dose)	Risk of QT prolongation, Baseline ECG and repeat at 2 weeks after commencement of treatment.
		Strong CYP3A4 inhibitor - Treatment modifications may be required. Please review all the patient's medications and supplements for potential medication interactions with the Clinical Pharmacist before commencement of eradication therapy.
		Monitor CHEM20
Oral Azithromycin	10 mg/kg orally once daily (maximum 500 mg/day)	Risk of QT prolongation. Baseline ECG and repeat at 2 weeks after commencement of treatment. Monitor CHEM20



Part 4. Fungal infections

Treatment of allergic bronchopulmonary aspergillosis (ABPA) in patients with cystic fibrosis

- Itraconazole dosing (Sporanox® brand):
 - Less than 12 years of age: Itraconazole oral 5 mg/kg/dose (max 200 mg/dose initially) twice daily (10 mg/kg/day) as starting dose.
 - More than 12 years of age: Itraconazole oral 2.5 mg/kg/dose (max 200 mg/dose initially) twice daily (5 mg/kg/day) as starting dose.
 - o ID approval required for itraconazole for ABPA treatment exceeding six (6) months.
 - o Prescribers to specify brand name and generic name on prescription to avoid confusion.
 - Sporanox® 100mg capsules and 10 mg/mL liquid are available on the List of approved medicines (LAM) and Pharmaceutical Benefit Scheme (PBS).
 - Lozanoc® (itraconazole 50mg) capsules <u>are not</u> interchangeable with Sporanox® (itraconazole 100mg) capsules or liquid.
 - The manufacturer of Lozanoc® reports that this product has higher bioavailability than other itraconazole capsules (e.g. Sporanox®). One capsule of Lozanoc 50 mg is therapeutically equivalent to one 100 mg capsule of conventional itraconazole capsules. The recommended dose for Lozanoc® is therefore half the recommended dose for conventional itraconazole capsules. Limited observational data exists in the paediatric population (Abbotsford J et al. JAC 2020)

Optimising azole absorption and levels

- o Due to significant difference in bioavailability, itraconazole capsules and liquid can't be used interchangeably.
- For Sporanox ® liquid preparation:
 - Take on empty stomach with an acidic drink (coca cola, orange juice).
- For Sporanox® capsule preparation:
 - Take with food and an acidic drink (coca cola, orange juice).
- Acid suppressing medications will affect stomach pH and reduce itraconazole absorption, consider clinical need for this agent if there is difficulty in obtaining therapeutic levels
- Consider compliance and how dose is being taken in relation to food/acidic drink if there is difficulty in obtaining therapeutic levels.

Therapeutic drug monitoring

- Itraconazole trough (pre-dose) level, 7 to 10 days from commencement of therapy as well as and 5 to 7 days after each dose adjustment.
- o Aim for trough level (taken 30 minutes before the morning dose) of 1000 to 2000 microgram/L.

Drug interactions

- Itraconazole is a potent inhibitor of CYP3A4 isoenzyme.
- o Treatment modifications may be required. Please review all the patient's medications and supplements for potential medication interactions with the Clinical Pharmacist before commencement of therapy.



Recommended adjustments

Ivacaftor (Kalydeco®)

Reduce the dose of Ivacaftor when initiating strong inhibitors of CYP3A4 (e.g. ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin and clarithromycin). Ivacaftor should be administered at a dose of:

- Children less than 14 kg: 50 mg twice a week only (space doses apart during week).
- Children 14 kg to 25 kg: 75 mg twice a week only (space doses apart during week).
- Children more than or equals to 25 kg: 150 mg twice a week only (space doses apart during week).
- With close monitoring of Itraconazole, Voriconazole or Posaconazole levels.
- Remember to re-review the Ivacaftor dose when the interacting drug is stopped.

When co-administered with moderate inhibitors of CYP3A4 (e.g. fluconazole, erythromycin), Ivacaftor should be administered at a dose of:

- Children less than 14 kg: 50 mg once daily.
- Children 14 kg to 25 kg: 75 mg once daily.
- Children more than or equal to 25 kg: 150 mg once daily.
- Remember to re-review the Ivacaftor dose when the interacting drug is stopped.

Ivacaftor/lumacaftor (Orkambi ®); Tezacaftor/ivacaftor (Symdeko®) and Elexacaftor/tezacaftor/ivacaftor (Trikafta®)

Consider alternative antifungal treatment options – seek Infection Specialist (ID) advice.

Anecdotal experience suggests high risk of itraconazole/voriconazole/posaconazole treatment failure in patients taking concomitant Ivacaftor / Lumacaftor; Tezacaftor/ivacaftor or Elexacaftor/ivacaftor.

o Cyclosporin, tacrolimus, sirolimus, warfarin, phenytoin

Monitor itraconazole levels and adjust accordingly.

Corticosteroids

Risk of growth failure in patients with CF on itraconazole reported (severe adrenal suppression observed). Monitor adrenal response carefully (31).

Useful drug interaction resources for comprehensive drug interaction information:

- Flockhart Cytochrome P450 Drug Interaction Table, Division of Clinical Pharmacology, Indianna University
- o Micromedex ® 2.0 Drug Interactions search. Truven Health Analytics ® (Available via CKN)
- o <u>UpToDate</u> Drug Interaction search.
- For all CFTR modulators, refer to Product information for up to date drug interaction information and advice on dose adjustments. Seek specialist advice for patients where medication interactions are possible.
- o Additional information available in the <u>CHQ-GDL-01075 Antifungal Prophylaxis and Treatment in</u> Paediatric Oncology Patients and other Immunocompromised Children.



- Alternative azole treatment options may include oral Voriconazole or oral Posaconazole.
 - o Discuss treatment options with ID team prior to commencing or changing therapy.
 - Therapeutic drug monitoring required discuss therapeutic target levels with ID team.
 - o ID approval required for oral Voriconazole and oral Posaconazole.
 - Please review all the patient's medications and supplements for potential <u>medication interactions</u> with the Clinical Pharmacist before commencement of therapy.

Part 5. Summary table antibiotic doses recommended for paediatric CF patients with normal renal function (including oral, IV and inhaled antibiotics)

Some IV medications require therapeutic drug monitoring (TDM). See table for recommendations.

Consider impact of patient/disease factors that may impact on TDM results, for example:

- Liver disease (risk of hepato-renal syndrome).
- Concomitant nephrotoxic medications (e.g. Tacrolimus, NSAIDs).
- Hydration status (consider oral fluid intake, fasting status, input/output including diarrhoea/vomiting).
- Age (impact of hormonal changes on body composition and organ function during adolescence).



Antimicrobial	Recommended starting doses for infants, children and adolescents with CF and normal renal function	ID approval required for	
	(For neonates or patients with renal/liver disease, seek specialist advice)	patients with CF (when fulfil indications above)	
Amikacin		Yes	
(Refer to Part 3 for more information)	Intravenous: Refer to CHQ-PMG-01294 Intravenous Aminoglycoside therapy (Amikacin, Gentamicin and Tobramycin)	res	
	Nebulised (DBL brand is appropriate for inhaled use):		
	Less than 6 years: Seek specialist advice.		
	Over 6 years of age: Inhale 500 mg twice daily		
	Use after physiotherapy		
	Monitor for bronchospasm. Consider using Salbutamol MDI pre-inhaled antibiotics as bronchodilator.		
	Prescription for Sodium Chloride 0.9% ampoules also required when prescribing inhaled Amikacin (required for dilution).		
	The Amikacin DBL 500mg/2mL injectable preparation is given via the nebulised route, using a suitable nebuliser with filter attachment (eg, Pari LC Plus with filter attachment).		
Amoxicillin / Clavulanate	Oral: 25 mg/kg/dose twice daily (maximum 875 mg/dose amoxicillin component)	No	
	Intravenous: 25 mg/kg/dose IV 6-hourly (maximum 1 g/dose amoxicillin component)	Yes	
Azithromycin	Oral: 10 mg/kg orally three times a week (anti-inflammatory for chronic lung disease) (max 500 mg/dose)	No	
	Oral: 10 mg/kg orally once daily (maximum 500 mg/day) (NTM treatment)		
	Risk of QT prolongation. Baseline ECG and repeat 2 weeks after commencement of treatment.	Yes	
Aztreonam	Intravenous: 50 mg/kg/dose 6-hourly (maximum 2 g/dose)	Yes	
	Nebulised (Aztreonam lysine for inhalation): More than 7 years of age: 75 mg inhaled three times a day	Yes (and SAS approval: Category A and B)	
Cefalexin	Oral: 30 mg/kg/dose three times daily (8 hourly) (maximum 1 g/dose)	No	
Cefazolin	Intravenous: 50 mg/kg/dose 8-hourly (maximum 2 g/dose)	No	
Cefepime	Intravenous: 50 mg/kg/dose 6-hourly (maximum 2 g/dose)	Yes	
Cefoxitin	Intravenous: 40 mg/kg/dose 6-hourly (maximum 2 g/dose)	Yes	
Ceftazidime	Intravenous: 100 mg/kg/dose 8-hourly (maximum 4 g/dose)	No (up to 14 days)	



Antimicrobial	Recommended starting doses for infants, children and adolescents with CF and normal renal function (For neonates or patients with renal/liver disease, seek specialist advice)	ID approval required for patients with CF (when fulfil indications above)
	Intravenous: 10 mg/kg/dose 8-hourly (maximum 400 mg/dose)	Yes
Ciprofloxacin	Oral: 20 mg/kg/dose twice daily (12 hourly) (maximum 1 g/dose) Oral ciprofloxacin has poor palatability, consider rounding doses to the nearest 125 mg (if appropriate based on weight) to reduce need to manipulate the dose form. For children unable to swallow tablets whole, discuss options to improve adherence with the Pharmacist. Monitor compliance closely. Risk of QT prolongation. Baseline ECG and repeat 2 weeks after commencement of treatment.	No
Clarithromycin	Oral: 7.5 mg/kg/dose twice daily (maximum 500 mg/dose) (NTM treatment). Risk of QT prolongation. Baseline ECG and repeat 2 weeks after commencement of treatment.	Yes
Clindamycin	Oral: 10 mg/kg/dose three times daily (8 hourly) (maximum 600 mg/dose). Oral Clindamycin has poor palatability, consider rounding doses to the nearest 150 mg (if appropriate based on weight) to reduce need to obtain part doses from capsules. For children unable to swallow capsules whole, discuss options to improve adherence with the Pharmacist or consider alternative treatment options – discuss with ID team. Monitor compliance closely.	Yes
Clofazimine	Oral: 1 to 5 mg/kg orally once daily (maximum 100 mg/day) Note: Children: Limited data, WHO recommendations for MDR-TB and XDR-TB are based on experience and expert opinion, and suggest 3 to 5 mg/kg/day (maximum 100 mg/day) (28) Risk of QT prolongation. Baseline ECG and repeat 2 weeks after commencement of treatment.	Yes (and SAS approval: Category A and B)
	Intravenous:	
	More than 5 years of age: 2 mg/kg/dose 8-hourly (Maximum 150 mg/dose) (maximum 8 mg/kg/ <u>day</u> for severe infections).	Yes
	Monitor for nephrotoxicity. Weekly CHEM20 and twice weekly urine dipsticks (monitor for proteinuria)	
	Nebulised:	
Colistin	1 to 2 years of age: 1 million units inhaled 12 hourly	No
	2 to 18 years of age: 1 to 2 million units inhaled 12 hourly	(If PsA resistant to
	(for eradication: 2 million units inhaled 12 hourly)	Tobramycin or failure of first line
	The dose administered of Colistin depends mostly on the concentration of the drug used and the tidal volume of the patient however the nebuliser characteristics are also very important and maintenance of the nebuliser is also critical (29). Seek CF consultant advice on nebulised dosing.	eradication regimen)
Doxycycline	Oral: More than 8 years of age: 2 mg/kg twice daily (maximum 100 mg/dose) Seek ID specialist advice for use in children less than 8 years of age.	Yes



Antimicrobial	Recommended starting doses for infants, children and adolescents with CF and normal renal function (For neonates or patients with renal/liver disease, seek specialist advice)	ID approval required for patients with CF (when fulfil indications above)
Ethambutol	Oral: 15 mg/kg once daily (Maximum 1200 mg/day) Dose based on lean body weight.	Yes
Flucloxacillin	Intravenous: 50 mg/kg/dose 6-hourly (maximum 2 g/dose) Oral: 25 mg/kg/dose four times a day (6-hourly) (maximum 1 g/dose)	No
Imipenem / Cilastatin	Intravenous: 25 mg/kg/dose IV 6-hourly (maximum 1g Imipenem component per dose) High incidence of nausea/vomiting – Imipenem / Cilastatin dose titration trialled in other patients with good effect. Pre-medicate with anti-emetics.	Yes
Itraconazole (Refer to Part 4 for more information)	Oral (Sporanox®): Less than 12 years of age: 5 mg/kg/dose (maximum 200 mg/dose initially) orally twice daily (10 mg/kg/day) as starting dose. More than or equal to 12 years of age: 2.5 mg/kg/dose (maximum 200 mg/dose initially) orally twice daily (5 mg/kg/day) as starting dose. Due to significant difference in bioavailability, Itraconazole capsules and liquid can't be used interchangeably. For Sporanox ® liquid preparation: Take on empty stomach with an acidic drink (coca cola, orange juice) For Sporanox® capsule preparation: Take with food and an acidic drink (coca cola, orange juice) TDM: Take trough (pre-dose) level 7 to 10 days from starting therapy. Aim for trough level (taken 30 minutes before the morning dose) of 1000 to 2000 microgram/L. Itraconazole is a potent inhibitor of CYP450 3A4 isoenzyme. Treatment modifications may be required. Please review all the patient's medications and supplements for potential medication interactions with the Clinical Pharmacist before commencement of therapy. Risk of QT prolongation. Baseline ECG and repeat 2 weeks after commencement of treatment.	No (up to 3 months for ABPA)
Lincomycin	Intravenous: 15 mg/kg/dose 6-hourly (max 1.2 g/dose)	Yes



Antimicrobial	Recommended starting doses for infants, children and adolescents with CF and normal renal function (For neonates or patients with renal/liver disease, seek specialist advice)	ID approval required for patients with CF
		indications above)
	Intravenous/ Oral:	
	Seek ID advice on dosing interval (May vary dependent on indication and duration of treatment course).	
	Less than 12 years of age: 10 mg/kg/dose 8 to 12 hourly	Yes
Linezolid	(maximum 600 mg/dose)	
	More than or equal 12 years of age: 10 mg/kg/dose 12-24 hourly (maximum 600 mg/dose)	
	Monitor FBC and lactate closely. May interact with tyramine containing foods and MAO inhibitors. Seek Pharmacist advice.	
	Intravenous: 40 mg/kg/dose 8-hourly (maximum 2 g/dose)	V
Meropenem	Monitor for thrush (oral and vaginal) in susceptible individuals	Yes
	Oral:	
Minocycline	More than 8 years of age: 4 mg/kg/dose (maximum 200 mg) as loading dose, then 2 mg/kg twice daily (Maximum 100 mg/dose).	Yes
	Seek ID specialist advice for use in children less than 8 years of age.	
	Intravenous: 10 mg/kg 24-hourly (maximum 400 mg/day)	
Moxifloxacin	Oral: 10 mg/kg once daily (maximum 400 mg/day)	Yes
	Risk of QT prolongation. Baseline ECG and repeat 2 weeks after commencement of treatment.	
Piperacillin/	Intravenous: More than 1 month of age:	No (up to 14 days)
Tazobactam	100 mg/kg/dose 6-hourly (maximum 4 g/dose piperacillin component)	(4p to 11 days)
	Oral:	
	10 to 20 mg/kg/dose once daily (maximum 450 mg/day if less than 40kg; maximum 600 mg/day if more than 40kg)	
Rifampicin	Check MRSA antibiotic susceptibilities prior to treatment and discuss with ID.	No (up to 14 days)
Timep.o	Rifampicin can interact with numerous medications.	The (up to 11 days)
	Pharmacy review prior to commencement.	
	Do not use Rifampicin if on any CFTR modulators or azole antifungals. Consider washout periods when starting/stopping therapy.	
Sodium fusidate	Oral : Sodium fusidate (tablets): 12 mg/kg/dose orally 8-hourly (maximum 500 mg/dose)	Yes
	Oral: Fusidic acid suspension: 15 mg/kg/dose orally 8-hourly (maximum 750 mg/dose)	Yes
	Fusidic acid oral suspension is not TGA registered and only available via the special access scheme (SAS). The suspension is <u>not</u> bioequivalent to sodium fusidate tablets.	(and SAS approval: Category A and B)



Antimicrobial	Recommended starting doses for infants, children and adolescents with CF and normal renal function (For neonates or patients with renal/liver disease, seek specialist advice)	ID approval required for patients with CF
		(when fulfil indications above)
Teicoplanin	Intravenous: 10 mg/kg/dose 12-hourly (maximum 800 mg/dose) for 3 doses (loading dose), then 10 mg/kg IV once daily (maximum 800 mg/day) for MRSA eradication.	Yes
reicopianin	Therapeutic drug monitoring (TDM) can be utilised if concerns about response to treatment. Please discuss with Infectious diseases team as TDM target may be dependent on MIC results.	165
	Intravenous: High incidence of nausea/vomiting – Tigecycline dose titration trialled in other patients with good effect. Pre-medicate with anti-emetics.	
Tigecycline	Day 1: (50% of optimal dose): 0.6 mg/kg IV 12-hourly (maximum 50 mg/dose)	
	Day 2: (75% of optimal dose) 0.6 mg/kg IV in the morning (maximum 50 mg/dose) 1.2 mg/kg IV at night (maximum 50 mg/dose)	Yes
	Day 3: (100% of optimal dose) 1.2 mg/kg IV 12-hourly (maximum 50 mg/dose, maximum 100 mg/day). If tolerated, continue on this dose.	
Tobramycin	Intravenous: Refer to CHQ-PMG-01294 Intravenous Aminoglycoside therapy (Amikacin, Gentamicin and Tobramycin)	No (up to 14 days)
Tobramycin	Nebulised / inhaled (use Tobramycin preservative free preparation):	No
inhaled	0 to 18 years of age: 300 mg inhaled twice daily (12-hourly)	
	or More than 6 years of age: TOBI® podhaler 112 mg (4 capsules) inhaled twice daily (12-hourly)	
Trimethoprim / Sulfamethoxazole	Intravenous: 5 mg/kg/dose 8-hourly (maximum 160 mg/dose Trimethoprim component) for 48 hours	Yes
	If renal function remains stable and urine pH more than 5.5, consider optimizing to dose to 5 mg/kg/dose IV 6-hourly (maximum 160 mg/dose Trimethoprim component). Monitor renal function and hydration status closely. Risk for renal toxicity and crystalluria.	
	Oral:	No
	Outpatient CF pulmonary optimization (non severe; no MRSA):	
	4 mg/kg/dose 12-hourly (maximum 320 mg/dose Trimethoprim component)	
	MRSA eradication/severe infection: 8 mg/kg/dose 12-hourly (maximum 320 mg/dose Trimethoprim component)	



Antimicrobial	Recommended starting doses for infants, children and adolescents with CF and normal renal function (For neonates or patients with renal/liver disease, seek specialist advice)	ID approval required for patients with CF (when fulfil indications above)
Vancomycin	Intravenous:	Yes
	Dose based on actual body weight. Perform TDM.	
	Please refer to the <u>CHQ Paediatric Medication Guideline</u> - <u>Vancomycin</u> for more information.	

Consultation

Key stakeholders who reviewed this version:

- Paediatric Respiratory Consultant Team (CHQ)
- Paediatric Infectious Diseases Consultant team (IMPS, CHQ)
- Pharmacist Advanced Antimicrobial Stewardship (CHQ)
- CHQ Medicines Advisory Committee endorsed 17/08/2023



List of abbreviations

Abbreviation	Definition
ABPA	Allergic bronchopulmonary aspergillosis
AFB	Acid fast bacilli
AMS	Antimicrobial Stewardship
AUC	Area Under the Curve
Bcc	Burkholderia cepacia complex
CF	Cystic fibrosis
CFTR	Cystic fibrosis transmembrane conductance regulator
CHEM20	A comprehensive metabolic panel is a group of blood tests, including electrolytes and liver function tests
CHQ	Children's Health Queensland
CKN	Clinicians Knowledge Network
Cmax	A pharmacokinetic measure used to determine drug dosing. Cmax is the maximum (or peak) serum concentration that a drug achieves in a specified compartment of the body after the drug has been administrated
Cmin	C24 predicted. A pharmacokinetic measure used to determine drug dosing. Cmin is the lowest concentration of a drug in the blood after a dose is given
ECG	Electrocardiogram
FBC	Full blood count
HITH	Hospital In The Home
IMPS	Infection Prevention and Management service
ID	Infectious diseases Team
IV	Intravenous
LAM	Queensland Health List of Approved of Medicines
MIC	Minimum Inhibitory Concentration is the lowest concentration of a chemical, usually a drug, which prevents visible growth of a micro-organism.
MRSA	Methicillin Resistant Staphylococcus Aureus
NSAIDs	Non-steroidal anti-inflammatory drugs
NTM	Non tuberculous mycobacteria
PBS	Pharmaceutical Benefit Scheme
PKPD	Pharmacokinetics and pharmacodynamics
PsA	Pseudomonas Aeruginosa
QCH	Queensland Children's Hospital
QT	QT prolongation is a measure of delayed ventricular repolarisation. Excessive QT prolongation can predispose the myocardium to the development of early after-depolarisations, which in turn can trigger re-entrant tachycardias such as Torsades de Pointes.
SAS	Special Access Scheme
TDM	Therapeutic drug monitoring
TOBI® podhaler	Inhaled Tobramycin 28mg capsule
WHO	World Health Organization



References and suggested reading

- 1. Zobell, J. T et al. Optimization of anti-pseudomonal antibiotics for cystic fibrosis pulmonary exacerbations: VI. Executive summary. Pediatr. Pulmonol.2013. doi: 10.1002/ppul.22757
- 2. Döring G et al. Treat of lung infection in patients with Cystic fibrosis: current and future strategies. Journal of Cystic Fibrosis 2012: 11: 461-479
- 3. Taketomo, C.K. (ed). (2018), In Pediatric Dosage handbook International, 25th edn, Lexi-Comp: USA.
- 4. Antibiotic Therapeutic Guidelines. (March 2018), Therapeutic Guidelines Committee, North Melbourne: Victoria.
- 5. Skov M, Hoiby N, Koch C. Itraconazole treatment of allergic bronchopulmonary aspergillosis in patients with cystic fibrosis. Allergy 2002;57(8):723-8.
- 6. Prentice AG, Glasmacher A. Making sense of itraconazole pharmacokinetics. J Antimicrob Chemother 2005;56 Suppl 1:i17-i22.
- 7. Hennig S, Wainwright CE, Bell SC, Miller H, Friberg LE, Charles BG. Population pharmacokinetics of itraconazole and its active metabolite hydroxy-itraconazole in paediatric cystic fibrosis and bone marrow transplant patients. Clin Pharmacol 2006 (IF:5.195)
- 8. Janssen Pharmaceutical Products LP. Sporanox® (Itraconazole) Oral Solution. http://www.fda.gov/cder/foi/label/2002/20657s7lbl.pdf: U.S. Food and Drug Administration; 2002.
- 9. Mayne Pharma International. Lozanoc ® (Itraconazole) capsules. https://www.mimsonline.com.au: Prescribing information: TGA approval date 16/04/2014 [accessed 14 Jan 2016]
- 10. Cystic fibrosis patient registry 2015 Annual data report. Bethesda, Maryland. Cystic Fibrosis Foundation 2016.
- 11. Cystic fibrosis patient registry 2014 Annual data report, Melbourne. Cystic Fibrosis Foundation Australia.
- 12.Ren CL, Morgan WJ et al Presence of MRSA in respiratory cultures from cystic fibrosis patients is associated with lower lung function. Paed Pulm, 2007; 42: 512-518
- 13. Dasenbrook EC, Merlo CA et al. Persistent MRSA and rate of FEV1 decline in Cystic Fibrosis. Am J Resp Crit Car Med 2008; 178: 814-821
- 14. Dasenbrook EC, Checkley W et al. Association between Respiratory tract MRSA and survival in Cystic Fibrosis. JAMA, June 2010; 303(23): 2386-2392
- 15.Lo DK, Hurley MN et al. Interventions for the eradication of MRSA in people with Cystic Fibrosis. Cochrane Database of Systematic Reviews 2015, Issue 2, Article CD009650
- 16. The UK Cystic Fibrosis Trust Infection Control Working Group. Methicillin Resistant Staphylococcus Aureus. April 2008.
- 17. Muhlebach MS, Beckett V et al. Microbiological efficacy of early MRSA treatment in Cystic Fibrosis in a randomised controlled trial. Thorax, June 2017; 72 318-326
- 18. Valliere's E, Rendall JC et al MRSA eradication of newly acquired lower respiratory infection in cystic fibrosis. ERJ Open Re, 2016;
- 19. Vanderhelst E, Meirleir L et al. Reply to Methicillin Staph Aureus. J Cystic Fibrosis 2013: 12: 183
- 20.Hall H, Gadhok R et al. Eradication of respiratory tract MRSA at a large adult cystic fibrosis centre. Respiratory Medicine (2015) 109: 357-363.
- 21. Vanderhelst E, Wachter E. Eradication of chronic methicillin-resistant Staphylococcus aureus infection in cystic fibrosis patients. An observational prospective cohort study of 11 patients. Journal of Cystic Fibrosis, Volume 12, Issue 6, Dec 2013: 612-616
- 22. Macfarlane M, Leavy L et al. Successful decolonisation of MRSA in paediatric patients with Cystic Fibrosis using a three strep protocol. J Hosp Infec 2007; 65; 231-236
- 23. Solis A, Brown D et al. MRSA in Children with Cystic Fibrosis: An eradication protocol. Paed Pulm 2003; 36: 189-195
- 24.Etherington C, Peckham DG, Conway SP, Denton M. Burkholderia cepacia complex infection in adult patients with cystic fibrosis is early eradication possible? J Cyst Fibros 2003;2(4):220-1



- 25. Horsley A, Webb K, Bright-Thomas R, et al. Can early Burkholderia cepacia Complex Infection in Cystic Fibrosis be Eradicated with Antibiotic Therapy? Front Cell Infect Microbiol 2011;1:18
- 26. Avgeri SG, Matthaiou DK, Dimopoulos G, et al. Therapeutic options for Burkholderia cepacia infections beyond cotrimoxazole: a systematic review of the clinical evidence. Int J Antimicrob Agents 2009; 33(5): 394-404
- 27.Leung JM, Olivier KN. Nontuberculous mycobacteria in patients with cystic fibrosis. Semin Respir Crit Care Med. 2013; 34 (1):124.
- 28. Haworth CS, et al. British Thoracic Society guidelines for the management of non-tuberculous mycobacterial pulmonary disease (NTM-PD). Thorax 2017;72:iii1–ii64. doi:10.1136/thoraxjnl-2017-210927
- 29.Buttini F, et al. Combinations of colistin solutions and nebulisers for lung infection management in cystic fibrosis patients. International Journal of Pharmaceutics 2016; 502: 242–248
- 30.Pamp SJ, et al.Tolerance to the antimicrobial peptide colistin in Pseudomonas aeruginosa biofilms is linked to metabolically active cells, and depends on the pmr and mexAB-oprM genes, Mol Microbiol, 2008; 68: 223-240
- 31. Albert AB, et al. An unusual cause of growth failure in cystic fibrosis: A salutary reminder of the interaction between glucocorticoids and cytochrome P450 inhibiting medication. Journal of Cystic Fibrosis. 2015; 14: e9–e11
- 32. Griffith DE, Brown-Elliott BA, Shepherd S, McLarty J, Griffith L, Wallace RJ Jr. Ethambutol ocular toxicity in treatment regimens for Mycobacterium avium complex lung disease. Am J Respir Crit Care Med. 2005 Jul 15;172(2):250-3
- 33. Yang HK et al. Incidence of toxic optic neuropathy with low-dose ethambutol. Int J Tuberc Lung Dis 2016; 20(2):261–264

Guideline revision and approval history

Version No.	Modified by	Amendments authorised by	Approved by
1.0 (replaces CHQ-GDL- 01059)	Paediatric Respiratory Consultant and Fellow Team Paediatric Infectious Diseases Consultant and Fellow team Antimicrobial Stewardship Pharmacist	Divisional Director Medicine	Executive Director Clinical Services (QCH)
1.1 21/07/2020	Paediatric Respiratory Consultant Team Paediatric Infectious Diseases Consultant team Antimicrobial Stewardship Pharmacist	Divisional Director Medicine	Executive Director Clinical Services (QCH)
2.0 08/12/2020	Paediatric Respiratory Consultant Team Paediatric Infectious Diseases Consultant team Antimicrobial Stewardship Pharmacist	CHQ Medicines Advisory Committee	Executive Director Clinical Services (QCH)
3.0 18/11/2021	Paediatric Respiratory Consultant Team Director of Ophthalmology Paediatric Infectious Diseases Consultant team Antimicrobial Stewardship Pharmacist	A/Director IMPS	Divisional Director Medicine
4.0 17/08/2023	Paediatric Respiratory Consultant Team Paediatric Infectious Diseases Consultant team Antimicrobial Stewardship Pharmacist	CHQ Medicines Advisory Committee	Executive Director Clinical Services (QCH)



cystic fibrosis, exacerbation, inpatient management, outpatient management, pseudomonas aeruginosa, allergic bronchopulmonary aspergillosis, ABPA, antimicrobial stewardship, HITH, hospital in the home, tobramycin, TOBI, amoxycillin-clavulanic acid, trimethoprim-sulfamethoxazole, piperacillin-tazobactam, ceftazidime, ciprofloxacin, colistin, ABPA, itraconazole, NTM, non tuberculous mycobacteria, Bcc, burkholderia cepacia, MRSA, methicillin resistant staphylococcus aureus, lincomycin, clindamycin, rifampicin, sodium fusidate, fusidic acid, amikacin, clofazimine, moxifloxacin, azithromycin, clarithromycin, cefoxitin, ethambutol, optic neuritis, imipenem/cilastatin, meropenem, minocycline, doxycycline, flucloxacillin, cefalexin, vancomycin, aztreonam, cefepime, moxifloxacin, teicoplanin, 01073



Accreditation references

NSQHS Standards (1-8): 3 Preventing and Controlling Healthcare-Associated Infection, 4 Medication Safety

ISO 9001:2015 Quality Management Systems: (4-10)

