GUIDELINE	
Cystic Fibrosis - Paediatric	
Scope (Staff):	Clinical Staff – Medical, Nursing, Pharmacy
Scope (Area):	Perth Children's Hospital (PCH)
Child Safe Organisation Statement of Commitment The Child and Adolescent Health Service (CAHS) commits to being a child safe organisation by meeting the National Child Safe Principles and National Child Safe Standards. This is a commitment to a strong culture supported by robust policies and procedures to ensure the safety and wellbeing of children at CAHS.	

This document should be read in conjunction with this DISCLAIMER

- These are empiric guidelines. Treatment in this group of patients is also guided by previous microbiology results and previous response to treatment. When not using the empiric guidelines due to either known microbiology or previous treatment response, please indicate this on the medication chart with reason. Please contact infectious diseases or clinical microbiology to discuss treatment at any stage.
- In patients who receive aminoglycoside (IV or inhaled) treatment, audiology should be arranged during the admission to monitor for adverse effects. Vestibular assessment should be performed according to the Burrow Test weekly whilst on aminoglycosides.
- **Burrow test**: This is a simple test that assists in early diagnosis of vestibular toxicity. With the patient seated and with the head kept still at 6 metres from the Snellen chart, determine their best visual acuity with both eyes open (no need to test eyes individually). Then do the same with examiner standing behind the patient and rotating the patient's head side to side at a rate of approximately one cycle per second. A normal person will lose less than or equal to 2 rows on the Snellen chart. Anything greater than this indicates an abnormality of the vestibulo-ocular reflex (i.e. bilateral vestibular injury). Record both baseline and during rotation results to compare with prior and future tests
- All patients should receive the annual influenza vaccine

CLINICAL SCENARIO	Usual duration	DRUGS/DOSES Standard Protocol	Monitoring
Exacerbation of Cystic Fibrosis	10 – 14 days	IV tobramycin 10mg/kg/dose (to a maximum dose of 750mg) once daily with subsequent doses based on area under the curve therapeutic drug monitoring. Ensure patients are well hydrated prior to commencement. **WITH** IV ceftazidime 50mg/kg/dose (to a maximum of 3 grams) 8 hourly **OR** IV piperacillin/tazobactam 100mg/kg/dose (to a maximum of 4 grams piperacillin component) 8 hourly Consideration may be given to a continuous IV infusion of piperacillin/tazobactam (300mg/kg/day to a maximum of 12 grams piperacillin component in 24 hours), 8 hourly IV piperacillin/tazobactam via Springfusor® OR 8 hourly IV ceftazidime via Springfusor® in suitable patients via Hospital in the Home (HiTH).	Tobramycin Area under the Curve (AUC) measurement on admission, after any dose change and weekly for duration of treatment. Weekly Full Blood Count (FBC), Electrolytes, Urea and Creatinine (EUC) and Liver Function Tests (LFTs). If no port is available or peripherally inserted central catheter (PICC) line does not bleed back – contact treating team. Monitoring for vestibular toxicity should occur whilst on IV tobramycin

<table>
<tr><th rowspan="2">CLINICAL SCENARIO</th><th rowspan="2">Usual duration</th><th colspan="2">DRUGS/DOSES</th><th rowspan="2">Monitoring</th></tr>
<tr><th colspan="2">Standard Protocol</th></tr>
<tr><td>Eradication of Pseudomonas aeruginosa in a child with Cystic Fibrosis</td><td>28 days (extended course may be considered)</td><td colspan="2">Eradication should be considered for all patients on the first isolation of Pseudomonas aeruginosa or after previous negative cultures from a sputum sample or bronchoalveolar lavage (BAL).

As for treatment of an exacerbation in a patient with Cystic Fibrosis (see above).

FOLLOWED BY

Inhaled tobramycin[a]
Children 6 months to 2 years old 150mg twice daily via nebuliser
Children 2 years and older 300mg twice daily via nebuliser. OR
Children 6 years and older 112mg (4 x 28mg capsules) administered twice daily via dry powder inhaler

AND/OR

Oral ciprofloxacin 15-20mg/kg/dose (to a maximum of 750mg) 12 hourly. Consider the following suggested dose bands below to allow rounding to the most appropriate tablet size.
<table><tr><th>Weight</th><th>Dose</th></tr><tr><td>< 6kg</td><td>20mg/kg twice daily (consider syrup formulation)</td></tr><tr><td>6kg to < 8.4kg</td><td>125mg twice daily</td></tr><tr><td>8.4kg to <11kg</td><td>187.5mg twice daily</td></tr><tr><td>11kg to <14kg</td><td>250mg twice daily</td></tr><tr><td>14kg to <17kg</td><td>312.5mg twice daily</td></tr><tr><td>17kg to <22kg</td><td>375mg twice daily</td></tr><tr><td>22kg to <28kg</td><td>500mg twice daily</td></tr><tr><td>28kg to <35kg</td><td>625mg twice daily</td></tr><tr><td>≥35kg</td><td>750mg twice daily</td></tr></table></td><td>For children on courses of oral antibiotics beyond 2 weeks of therapy recommend FBC, EUC and LFTs be done at 2 weeks and repeated if abnormal.

ciprofloxacin: patients should be instructed to alert team if any symptoms of arthropathy (e.g. bone or joint symptoms)</td></tr>
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CLINICAL SCENARIO	Usual duration	DRUGS/DOSES Standard Protocol	Monitoring
Eradication of *Staphylococcus aureus* or methicillin resistant Staphylococcus aureus (MRSA) in a child with Cystic Fibrosis	10-14 days	Decolonisation for patients and family is recommended as part of the eradication. Apply nasal mupirocin 2% ointment to nares twice daily for 5 days **AND** 2% chlorhexidine (for children ≥ 3 months old) as a daily body wash for **5 days**. Refer to: MRSA and MSSA Guidelines for Staphylococcal decolonisation for further information. **IN CONJUNCTION WITH** Oral rifampicin[b] 15mg/kg/dose (to a maximum of 600mg) once daily **AND** Oral sodium fusidate[c] tablets For children <5 years: use cotrimoxazole (as below) Child 5-12 years: 250mg 8 hourly. Child ≥ 12 years: 500mg given 8 hourly. ***OR*** Monotherapy: Oral cotrimoxazole 4mg/kg/dose (to a maximum of 160mg trimethoprim component) 12 hourly If either of these agents are not tolerated, contact infectious diseases for advice. **If the above regimen fails, repeat course with or without** Inhaled vancomycin Children ≥4 years: 4mg/kg/dose (to a maximum of 250mg) four times a day for 10-14 days Contact infectious diseases for advice on children <4 years of age.	FBC, EUC, LFTs only after two weeks on treatment (i.e. if course is repeated). Cease treatment if thrombocytopenia or hepatotoxicity occurs.

CLINICAL SCENARIO	Usual duration	DRUGS/DOSES Standard Protocol	Monitoring
Prevention of frequent exacerbations in a child with Cystic Fibrosis	Up to 12 months	**CONSIDER** Oral azithromycin as an anti-inflammatory agent: Child ≥1 – 6 years: 10mg/kg/dose (to a maximum of 250mg) three times a week Child ≥ 6 years: 25-40kg: 250mg three times a week Child ≥ 6 years: ≥ 40kg: 500mg three times a week **OR** Children ≥1 year: 30mg/kg/dose (to a maximum of 1.5gram) once a week Exclude non-tuberculosis mycobacterial infection prior to initiation	LFTs and FBC monitored every 3 months on extended courses.

CLINICAL SCENARIO	Usual duration	DRUGS/DOSES Standard Protocol	Monitoring
Allergic Broncho-pulmonary Aspergillosis (ABPA)		Diagnosis is based on both clinical findings and immunological investigations: • Aspergillus infection. Aspergillus isolated from a respiratory specimen or precipitins/IgG to *A. fumigatus* • Clinical signs/symptoms: clinical deterioration not attributable to another aetiology OR new abnormalities on chest imaging unresponsive to antibiotic therapy • Allergic sensitisation: Serum total IgE >500 international units/mL and positive skin prick testing (SPT) *OR* IgE to *A. fumigatus* **Once ABPA confirmed:** Systemic glucocorticoids as first line therapy. **For refractory or severe cases consider addition of:** Oral Itraconazole[d] with therapeutic drug monitoring (adjunctive therapy or as a steroid sparing agent) in discussion with Infectious Diseases: Itraconazole[d] (**Lozanoc®)** capsules: 5mg/kg/dose (to a maximum of 150mg) twice daily. **OR** Itraconazole[d] (**Sporanox®)** liquid: 5mg/kg/dose (to a maximum of 300mg) twice daily **Note:** Itraconazole interacts with many medications including ivacaftor / lumacaftor. Contact Pharmacy for advice.	FBC, EUC and LFTs performed monthly. Itraconazole levels should be measured 7 days after commencing and after any dose change. Target levels should be ≥1mg/L. **Once the dose is stable, levels should be checked monthly.**
Staphylococcus aureus prophylaxis in early Cystic Fibrosis life (<5 years)		Oral flucloxacillin 12.5mg/kg/dose (to a maximum of 500mg) given 6 hourly **OR** Oral amoxicillin/clavulanic acid 25mg/kg/dose (based on amoxicillin component - to a maximum of 875mg amoxicillin) given 12 hourly Therapy should be ceased if patient becomes colonised.	Annual FBC, EUC, LFTs whilst on prophylactic doses.

a. Inhaled tobramycin is available in multiple formulations. Any prescriptions for the Tobi® brand of products must fit criteria as per Formulary 1 - Paediatric
b. Rifampicin and fusidic acid/sodium fusidate are red/restricted ChAMP agents. However, when used in accordance with this guideline, prescribers do not need approval from infectious diseases or clinical microbiology prior to prescribing.
c. Fusidic acid liquid is available via the Special Access Scheme. Children 1 month to 18years; 15mg/kg/dose (to a maximum of 750mg) 8 hourly. Due to differences in absorption, 250mg of fusidic acid is therapeutically equivalent to 175mg sodium fusidate. Contact Pharmacy for further information.
d. The three available itraconazole formulations (Sporanox® and Lozanoc® capsules and Sporanox liquid®) are NOT interchangeable. Only Lozanoc® capsules and Sporanox liquid are kept at PCH. ALL prescriptions should state the formulation and brand required. Lozanoc® is the preferred brand of capsule due to less variability of bioavailability.

Related internal policies, procedures and guidelines
Antimicrobial Stewardship Policy (PCH Website)
ChAMP Empiric Guidelines

References

1. Goldfarb S. Cystic Fibrosis. BMJ Best Practice. March 2020. http://bestpractice.bmj.com/best-practice.html. Last accessed 21st April 2020.
2. Therapeutic Guidelines Ltd. eTG complete [online]. West Melbourne: Therapeutic Guidelines Ltd; accessed online 21st April 2020.
3. Weaver LT, Green MR, Nicholson K, Mills J, Heeley ME, Kuzemko JA, Austin S, Gregory GA, Dux AE, Davis JA. Prognosis in cystic fibrosis treated with continuous flucloxacillin from the neonatal period. Archives of disease in childhood. 1994 Feb 1;70(2):84-89.
4. Valery PC, Morris PS, Byrnes CA, Grimwood K, Torzillo PJ, Bauert PA, et al. Long-term azithromycin for Indigenous children with non-cystic-fibrosis bronchiectasis or chronic suppurative lung disease (Bronchiectasis Intervention Study): a multicentre, double-blind, randomised controlled trial. The Lancet Respiratory Medicine. 2013;1(8):610-20.
5. Wilms E, Touw D, Heijerman HM, van der Ent C. Azithromycin maintenance therapy in patients with cystic fibrosis: A dose advice based on a review of pharmacokinetics, efficacy, and side effects. Pediatric Pulmonology. 2012;47(7):658-65.

6. Royal Australian College of General Practitioners, Pharmaceutical Society of Australia, Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists. AMH: Children's Dosing Companion. Adelaide: Australian Medicines Handbook Pty Ltd; 2022.

This document can be made available in alternative formats on request for a person with a disability.

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