Guideline
Paediatric Respiratory Antibiotic Card: Empirical antimicrobial therapy for patients with Cystic Fibrosis and Non-CF Bronchiectasis

<table>
<thead>
<tr>
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<td>Executive sponsor</td>
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Purpose

This guideline provides recommendations regarding best practice for empirical antimicrobial therapy for paediatric patients with Cystic Fibrosis (CF) and non-CF bronchiectasis, for inpatient and outpatient management.

Scope

This guideline provides information for CHQ staff caring for paediatric CF and non-CF bronchiectasis patients.

Related documents

Procedures, Guidelines, Protocols

- CHQ Guideline: Paediatric Therapeutic Drug monitoring of Tobramycin and Gentamicin
- CHQ@Home manual
- CHQ@Home Outpatient Parenteral Antimicrobial Therapy Prescribing, Administration and monitoring guideline
- CHQ Procedure_01035 Antimicrobial Restriction Procedure
- Antimicrobial Restriction list
Guideline

Paediatric Respiratory Antibioticcard: Empirical antimicrobial therapy for patients with Cystic Fibrosis and Non-CF Bronchiectasis:

Figure 1: Cystic Fibrosis Exacerbation – Pseudomonas aeruginosa (PsA) negative

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<thead>
<tr>
<th>Outpatient Management (or Empirical oral antibiotics management when microbiology not known/awaited)</th>
<th>Inpatient Management</th>
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<tbody>
<tr>
<td><strong>Amoxicillin-Clavulanic acid #</strong>&lt;br&gt;25mg/kg/dose ORAL 12-hourly of DUO preparation (Max 875mg Amoxicillin component/dose)<strong>&lt;br&gt;</strong>&lt;br&gt;<strong>OR</strong>&lt;br&gt;<strong>Trimethoprim-Sulfamethoxazole #&lt;br&gt;4mg/kg/dose ORAL 12-hourly (Max 160mg/dose Trimethoprim component)</strong>&lt;br&gt;Note: Higher doses may be used in severe infection – seek ID advice&lt;br&gt;<strong>Comment:</strong>&lt;br&gt;<strong># Alter therapy based on previous microbiology if available</strong></td>
<td><strong>Piperacillin-Tazobactam</strong>&lt;br&gt;100mg/kg/dose IV every 6-hourly (Max 4gram/dose Piperacillin component)&lt;br&gt;(if &lt; 1 month: every 8 hours)<strong>&lt;br&gt;<strong>If microbiology unknown/awaited/failure on oral antibiotic therapy, ADD</strong>&lt;br&gt;Tobramycin 10 mg/kg IV once daily (max 640mg for the initial dose of Tobramycin)#&lt;br&gt;<strong>Comment:</strong>&lt;br&gt;</strong># Tobramycin 2 &amp; 6 hour post dose levels after 1st dose (for AUC calculation)**</td>
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Note: Continuous infusion for certain beta lactam antibiotics in hospital may be considered to facilitate early HITH discharge, where appropriate. Please refer to [CHQ@Home Outpatient Parenteral Antimicrobial Therapy Prescribing, Administration and monitoring guideline](available via AMS Intranet Website) for further information.

CHQ-GDL-01059 – Paediatric Respiratory Antibioticcard- Empirical antimicrobial therapy for patients with Cystic Fibrosis and Non-CF Bronchiectasis
Empirical antimicrobial therapy for Cystic Fibrosis patients (continued)

Figure 2: Cystic Fibrosis – Pseudomonas aeruginosa (PsA) Eradication

Note: Continuous infusion for certain beta lactam antibiotics in hospital may be considered to facilitate early HITH discharge, where appropriate. Please refer to CHQ@Home Outpatient Parenteral Antimicrobial Therapy Prescribing, Administration and monitoring guideline.
Empirical antimicrobial therapy for Cystic Fibrosis patients (continued)

Figure 3: Cystic Fibrosis with chronic Pseudomonas aeruginosa (PsA) infection

Cystic Fibrosis (CF) with chronic Pseudomonas aeruginosa (PsA) infection

- **Outpatient Management**
  - Nebulised TOBI® 300 mg
    - 12 hourly (or Inhaled TOBI® podhaler 112 mg (4 capsules))
    - twice daily for 4 weeks
    - with or without
  - Oral Ciprofloxacin 20mg/kg/dose 12-hourly (Max 1gram/dose)
  - **Comment:**
    - If on cyclical inhaled TOBI®; may consider:
    - Oral Ciprofloxacin 20mg/kg/dose 12-hourly (Max 1gram/dose)
  - **PLUS**
    - Inhaled Colistin
    - 1 to 2 million units/dose 12hourly

- **Inpatient Management**
  - **Piperacillin-Tazobactam**
    - 100mg/kg/dose IV every 6-hourly (Max 4gram/dose Piperacillin component)
    - (If < 1 month: every 8 hours)
  - **WITH**
    - **Tobramycin** 10 mg/kg IV once daily (max 640mg for the initial dose of Tobramycin)
  - **Comment:**
    - **Ceftazidime 100 mg/kg/dose 8-hourly (Max 4 grams/dose)** may be considered instead of Piperacillin-Tazobactam if no concomitant *Staphylococcus aureus* infection.
    - # Tobramycin 2 & 6 hour post dose levels after 1st IV dose (for AUC calculation)

Note: Continuous infusion for certain beta lactam antibiotics in hospital may be considered to facilitate early HITH discharge, where appropriate. Please refer to [CHQ@Home Outpatient Parenteral Antimicrobial Therapy Prescribing, Administration and monitoring guideline](available via AMS Intranet Website) for further information.

CHQ-GDL-01059 – Paediatric Respiratory Antibiocard- Empirical antimicrobial therapy for patients with Cystic Fibrosis and Non-CF Bronchiectasis
Treatment of allergic bronchopulmonary aspergillosis (ABPA) in patients with cystic fibrosis

- **Itraconazole Dosing (Sporanox ® brand):**
  - <12 years of age: Itraconazole oral 5mg/kg/dose (max 200mg/dose) TWICE DAILY (10mg/kg/day) as starting dose
  - >12 years of age: Itraconazole oral 2.5mg/kg/dose (max 200mg/dose) TWICE DAILY (5mg/kg/day) as starting dose
  - Prescribers to specify brand name and generic name on prescription to avoid confusion
    - Sporanox ® 100mg capsules and 10mg/mL liquid available on the LAM and PBS
    - Lozanoc ® (itraconazole 50mg) capsules are not interchangeable with Sporanox ® (itraconazole 100mg) capsules and are not listed on the LAM or PBS.
    - Lozanoc® has a higher bioavailability than other itraconazole capsules (for example: 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.

- **Optimising azole absorption and levels**
  - Note: Itraconazole capsules and liquid can’t be used interchangeably – significant difference in bioavailability
  - For liquid preparation: Take on empty stomach with an acidic drink (coca cola, orange juice)
  - For capsule preparation (Sporanox ®): Take with food and an acidic drink (coca cola, orange juice)

- **Therapeutic drug monitoring:**
  - Itraconazole trough (pre-dose) level 7 to10 days from starting therapy. Aim for trough level 500 to 1000microgram/L.

- **Drug interactions:**
  - Itraconazole is a potent inhibitor of CYP450 3A4 isoenzyme.
  - **Recommended adjustments:**
    - **Ivacaftor:**
      - Reduce the dose of Ivacaftor prior to initiating itraconazole:
      - When coadministered with strong inhibitors of CYP3A4 (e.g. ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin and clarithromycin), Ivacaftor should be administered at a dose of 150 mg twice a week (in children >6 years of age), with close monitoring of Itraconazole, Voriconazole or Posaconazole levels.
      - When coadministered with moderate inhibitors of CYP3A4 (e.g. fluconazole, erythromycin), Ivacaftor should be administered at a single daily dose of 150 mg (in children >6 years of age).
    - **Cyclosporin, tacrolimus, sirolimus, warfarin, phenytoin:** monitor levels

- **Useful drug interaction resources for comprehensive drug interaction information:**
  - Flockhart Cytochrome P450 Drug Interaction Table, Division of Clinical Pharmacology, Indiana University
  - Micromedex ® 2.0 Drug Interactions search. Truven Health Analytics ® (Available via CKN)
Empirical antimicrobial therapy for patients with non-CF bronchiectasis

Figure 4: Non-CF Bronchiectasis exacerbation

- Non-CF Bronchiectasis exacerbation
  - Outpatient Management
    - Amoxycillin-Clavulanic acid
      - 25mg/kg/dose ORAL 12-hourly of DUO preparation (Max 875mg Amoxycillin component/dose)
      - OR
    - Trimethoprim-Sulfamethoxazole
      - # 4mg/kg/dose ORAL 12-hourly (Max 160mg/dose Trimethoprim component)
    - Comment:
      # Alter therapy based on previous microbiology if available
  - Inpatient Management
    - Cefotaxime IV 50mg/kg/dose 6-hourly (Max 2gram/dose)
      - OR
    - Ceftriaxone IV 100mg/kg once daily (Max 4gram/day)
    - Comment:
      # Alter therapy based on previous microbiology if available
Consultation

Key stakeholders who reviewed this version:
- Paediatric Respiratory Consultant Team (CHQ)
- Paediatric Infectious Diseases Consultant team (IMPS, CHQ)
- Antimicrobial Stewardship Pharmacist (CHQ)

List of abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>ABPA</td>
<td>Allergic bronchopulmonary aspergillosis</td>
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<td>AMS</td>
<td>Antimicrobial Stewardship</td>
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<tr>
<td>AUC</td>
<td>Area Under the Curve</td>
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<td>CF</td>
<td>Cystic fibrosis</td>
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<td>CHQ</td>
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<td>HITH</td>
<td>Hospital In The Home</td>
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<td>Infection Prevention and Management service</td>
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<td>IV</td>
<td>Intravenous</td>
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<tr>
<td>PO</td>
<td>Per Oral</td>
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<tr>
<td>PsA</td>
<td>Pseudomonas Aeruginosa</td>
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<tr>
<td>TOBI®</td>
<td>Nebulised Tobramycin 300mg/5mL</td>
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<tr>
<td>TOBI® podhaler</td>
<td>Inhaled Tobramycin 28mg capsule</td>
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References and suggested reading

## Guideline revision and approval history

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<th>Version No.</th>
<th>Modified by</th>
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<td>Paediatric Respiratory Consultant Team (RCH) Paediatric Infectious Diseases Consultant team (IMPS, RCH) Antimicrobial Stewardship Pharmacist (RCH)</td>
<td>Medicines Advisory Committee (MAC)</td>
<td>General Operations Manager</td>
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<td>Paediatric Respiratory Consultant Team (LCCH) Paediatric Infectious Diseases Consultant team (IMPS, LCCH) Antimicrobial Stewardship Pharmacist (LCCH)</td>
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### Keywords
- respiratory antibiocard, cystic fibrosis, non-CF bronchiectasis, exacerbation, inpatient management, outpatient management, pseudomonas aeruginosa, allergic bronchopulmonary aspergillosis, antimicrobial stewardship, DUG, Drug Use Guideline, cefotaxime, ceftriaxone, tobramycin, TOBI, amoxycillin-clavulanic acid, trimethoprim-sulfamethoxazole, piperacillin-tazobactam, ceftazidime, ciprofloxacin, colistin, ABPA, itraconazole

### Accreditation references
- EQuIP National Standard: 3, 1, 4