Alder Hey Children's NHS Foundation Trust

Cystic Fibrosis

Antimicrobial guidelines

(for use by Alder Hey and its network clinics)

Version 3 (Update 2022)

Guidelines compiled by:

Andrew Lilley (Lead Pharmacist – Respiratory) andrew.lilley@alderhey.nhs.uk

Rachel Rowley (Specialist Paediatric Pharmacy – Cystic Fibrosis)

Inhaled therapy guidelines reviewed by:

Adam Walsh (Clinical Specialist Physiotherapist – Cystic Fibrosis)

Contributions made by:

Prof Kevin Southern (Lead consultant Alder Hey CF service)

Prof Paul McNamara (Consultant Respiratory Paediatrician)

Elinor Burrows (Consultant Nurse – CF)

Dr Rebecca Thursfield (Consultant Respiratory Paediatrician)

Dr Claire Halfhide (Consultant Respiratory Paediatrician)

Dr Sarah Mayell (Consultant Respiratory Paediatrician)

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Introduction

Antibiotic therapy for patients with CF is directed at preventing, eradicating, or controlling respiratory infections. The appropriate use of effective antibiotics in these situations has been a major reason for the decreased respiratory morbidity and increased longevity seen over the last several decades.

CF Trust May 2009

These guidelines contain the recommended medications and specific doses for the treatment of infection in cystic fibrosis at Alder Hey and our satellite clinics. Doses are higher than in non CF patients. This is due to altered pharmacokinetics in CF patients of the medications.

Doses containing within this document may vary from those found in the BNFc. These are generated from clinical experience as well as clinical papers. Many medications are being used 'off label' and should be treated as such.

2.Prophylaxis against infection

2.1 Staphylococcus aureus

2.1.1 Flucloxacillin

Contraindications – Penicillin allergy (seek advice from regional centre for alternative treatment)

Caution – hepatic dysfunction (seek advice from regional centre)

Preparations available –

- **Liquid**
  - 125mg/5ml
  - 250mg/5ml ***using higher strength formulation favoured due to poor palatability of liquid**
- **Capsules**
  - 250mg
  - 500mg

Monitoring requirements – LFTs at annual review

Dosage

Age	Birth to 3 yrs	3yrs onwards
Dosage[1]	**125mg BD**	**50mg/kg BD max 1g (round to most appropriate dosage form i.e 50mg for liquid or 250mg for capsules)**

Duration of course – Until three years old where it will reviewed at annual review.

Note the large increase in under/over three dose. Those over the age of three need larger dose to suppress staphylococcal growth if they do indeed need to remain on prophylaxis due to frequent infection

SOME PATIENTS MAY STILL BE ON OLD DOSING REGIMEN AND SHOULD NOT BE SWITCHED OVER IF SUFFICIENT CONTROL NOTED ON CLINCAL REVIEW

[1] CF trust - Antimicrobial guidelines and BNFc 2020/21

2.2 Haemophilus Influenza

In those patients who have had three positive cultures within a 12 month period contact the regional centre for advice regarding long term treatment. If the decision is taken to switch treatment (from other prophylaxis agent) cefaclor is the preferred option. Please note this change is not always necessary and will be made on an individual basis.

2.2.1 Cefaclor

Contraindications – Penicillin allergy (seek advice from regional centre)

Preparations available –

- **Liquid**
  - 125mg/5ml
  - 250mg/5ml
- **MR tablets**
  - 375mg

Monitoring requirements – None

Dosage

Age	Birth to 1 yr	1-7yrs	>7yrs
Dosage[2] (Normal release)	**125mg TDS**	**250mg TDS**	**500mg TDS**
Dosage (Modified release)[3]		**375mg BD**	**750mg BD**

Duration of therapy – Review at annual review clinic. If no clinical need treatment should be stopped. Consider switching patient back to flucloxacillin prophylaxis based on clinical need for Staph. aureus prophylaxis.

[2] BNFc 2020/21

[3] Clinical experience of Alder Hey team

3. Treatment of cough

3.1 Empirical treatment (oral therapy)

In those patients **with no known pathogen** who develop a **new cough** and in whom respiratory cultures are not informative, broad spectrum treatment should be used. **If after five days (or if any concerns from parent)** patient is not improving a respiratory culture should be taken and second line therapy should be considered. If no improvement seen after further 5 days bronchoscopy and IV therapy should be considered as per 3.2

3.1.1 Amoxicillin (first line)

Contraindications – Penicillin allergy (azithromycin alternative)

Preparations available –

- **Liquid**
  - 125mg/5ml
  - 250mg/5ml
- **Capsules**
  - 250mg
  - 500mg

Dose

Age	Birth to 11 months	1-4 years	5-11 years	12-17 years
Dosage[4]	125mg TDS	250mg TDS	500mg TDS	500-1000mg TDS

Monitoring requirements – None

Duration – See notes above. After 14 days patient should be symptom free. If symptoms persist contact regional clinic for advice.

[4] BNFc 2020/21 and Clinical experience of Alder Hey team

3.1.2 Co-amoxiclav (second line)

Contraindications – Penicillin allergy (seek advice from regional team for alternative)

Preparations available

- Liquid
  - Co-amoxiclav duo 400/57 per 5ml (recommended to improve compliance)
  - 125/31 per 5 ml (for doses see BNFc)
  - 250/62 per 5 ml (for doses see BNFc)
- Tablets – Use not currently recommended (see below)

Age	Birth to 23 months	2-6 years	7-12 years	12-17 years
Dosage *C-A Duo 400/57*[5]	**0.3ml/kg BD**	**5ml BD**	**10ml BD**	**10ml TDS**
Emerging evidence shows the ratio of amoxicillin to clavulanic acid contained in tablets is not effective against resistant respiratory tract infections. Therefore tablets are not recommended.				

Monitoring requirements – If long term use monitor LFTs

Duration – See notes above. After 14 days patient should be symptom free. If symptoms persist contact regional clinic for advice.

3.1.3 Azithromycin (Third line or first line in penicillin allergy)

Preparations available –

- **Liquid**
  - 200mg/5ml
- **Tablets**
  - 250mg
  - 500mg

Monitoring requirements – None

Dosage

Age	All ages
Dosage[6]	**10mg/kg OD (max 500mg)**

Duration – 5 days continuous therapy

[5] BNFc 2020/21 and Clinical experience of Alder Hey team
[6] BNFc 2020/21

3.2 Empirical treatment (IV therapy)

3.2.1 Ceftriaxone

Contraindications – Penicillin allergy (seek regional centre advice)

Dose

Age	1 month – 18 years
IV Dosage[7]	50mg/kg max 2g OD (if severe infection suspected increase to 80mg/kg max 4g OD to be infused over 30 mins)

Duration – 14 days (although may vary with clinical presentation). Always review at 72 hours for possible oral step down as per local antimicrobial stewardship protocols.

[7] BNFc 2020/21

4. Treatment of known respiratory pathogens

In those patients where cultures are available therapy should always be targeted accordingly.

4.1 Staphylococcus aureus infection

4.1.1 Flucloxacillin (oral) treatment dose

If respiratory cultures show S.aureus is present, flucloxacillin is the first line agent (**if sensitive on culture)**. If patient is currently on long term prophylaxis with flucloxacillin, increase to treatment dose (see below) for 14 days. Additionally, check compliance to prophylaxis and ensure still on an appropriate dose for age/weight. **If respiratory cultures demonstrate resistance to flucloxacillin see** 4.11 (MRSA)

Contraindications – Penicillin allergy (clarithromycin alternative see 4.3.1**)**

Preparations available –

- **Liquid**
  - 125mg/5ml
  - 250mg/5ml
- **Capsules**
  - 250mg
  - 500mg

Dose

Age	Birth to 11 months	1-4 years	5-11 years	12-17 years
Dosage[8]	125mg QDS	250mg QDS	500mg QDS	500-1000mg QDS
	Note total daily dose can be given in three divided doses if required Total daily dose of treatment may be similar to that of prophylactic however dose needs to be spread out throughout the day to have a bactericidal ('killing') effect not just a bacteriostatic ('suppressive') effect			

Monitoring requirements – None

Duration – 14 days

After treatment is complete check compliance with prophylaxis treatment and ensure dose is correct for age/weight before restarting

[8] BNFc 2020/21

4.2 Haemophilus influenza, Streptococcus pneumoniae or Moraxella catarrhalis

Treatment should be based on sensitivities however the following are usually recommended

4.2.1 Amoxicillin (first line) – See 3.1.1

4.2.2 Co-Amoxiclav (second line) – See 3.1.2

4.2.3 Ceftriaxone (Third line) see 3.2.1

4.3 Mycoplasma, Chlamydia or Legionella *spp*

4.3.1 Clarithromycin

Preparations available

- **Liquid**
  - 125mg/5ml
  - 250mg/5ml
- **Tablets**
  - 250mg

Dose

Age/ Weight	Birth to 11 years					12-17 years
	Under 8kg	8-11kg	12-19kg	20-29kg	30-40kg	
Dosage[9]	7.5mg/kg BD	62.5mg BD	125mg BD	187.5mg BD	250mg BD	500mg BD

Monitoring requirements – None

Duration – 14 days

4.4 Klebsiella, E.Coli, Proteus, Morganella, Citrobacter, Acinetobacter, Enterobacter on culture and has symptomatic cough

Due to high levels of resistance in this group treatment choice should always be guided by sensitives. Appropriate doses of medications can be found within this document.

[9] BNFc 2020/21

4.5 New growth of Pseudomonas aeruginosa

A 'new growth' of PsA is in those patients in whom PsA has been isolated for the first time OR patients who have **not** been on nebulised therapy for 6 months.

The following regimes should be followed

4.5.1 Asymptomatic patients (new growth)

Day 0 – Start patient on ciprofloxacin (or chloramphenicol under specific circumstances) **AND** nebulised colistin (see 4.7.1)

Day 14 – Repeat sputum culture

- If clear continue nebulised treatment for 3 months and stop ciprofloxacin on day 21
- If persists continue ciprofloxacin for a total of 3 months in combination with nebulised colistin (repeat respiratory culture at day 42)

Day 42 – Repeat sputum culture

- If respiratory culture clear continue ciprofloxacin and nebulised colistin for three months **in total**
- If respiratory culture not clear discuss with regional CF centre

Day 90 – Repeat sputum culture

- If culture is clear stop all treatment
- If persists discuss case with regional CF centre **(DO NOT DELAY TREATMENT)**. Continue nebulised colistin/tobramycin until such time that culture is clear for 12 months. IV antimicrobial therapy may be required as per regional CF centre advice (see 4.6)

4.5.1a Ciprofloxacin

Preparations available

- Liquid
  - 250mg/5ml
- Tablets
  - 100mg
  - 250mg (can be split into 62.5mg segments)
  - 500mg

Age	Birth to 12 months	1-12years	>12 years
Dosage [10]	**15mg/kg BD**	**20mg/kg BD (max 750mg)**	**750mg BD**

[10] BNFc 2020/21

4.5.1b Chloramphenicol

In those patients who have either not responded to ciprofloxacin **or** have allergy to quinolones **and** IV therapy is not favourable chloramphenicol oral can be used.

Contraindications - porphyria

Preparations available

- Capsules
    - 250mg (can be opened and contents dispersed in water or sprinkled on yoghurt)

Age	>6 years
Dosage[11]	**12.5mg/kg QDS (in severe resistant infection dose can be increased to 25mg/kg QDS)** **Always round dose to nearest 250mg capsule** **FBC should be monitored after D7, D21 and monthly if long term**

4.5.2 Symptomatic patients (new growth)

All symptomatic patients should be discussed with regional CF centre for consideration for bronchoscopy. Patients will usually require 2 weeks of IV therapy as below.

4.5.2a Most recent respiratory cultures indicate a growth of Pseudomonas aeruginosa and all strains sensitive to ceftazidime

1st line combination of ceftazidime and tobramycin

Age	1 month – 18 years
Dosage ceftazidime[12]	**IV 50mg/kg max 3g TDS**
Dosage Tobramycin[13]	**(Only to be initiated once a satisfactory U+E, LFT and FBC has been confirmed)** **Even if had bloods pre bronchoscopy these need to be repeated when returning to ward** **(Dose should be prescribed ideally for between 8am to 2pm. This is to aid renal clearance due to better daytime hydration)** **IV 10mg/kg max 600mg OD** **(Levels should be taken 20-24 hours post dose on D2 and D7 OR as per local guidelines)**

Duration: 14 days

[11] Based on dosage found in BNFc 2020/21 and Royal Brompton CF antimicrobial guideline 2017
[12] BNFc 2020/21

4.5.2b Most recent respiratory cultures indicate a growth of Pseudomonas aeruginosa and strains show **resistance** to ceftazidime **OR** lack of clinical improvement whilst on ceftazidime

Choose a combination of two antimicrobials that the organism(s) are sensitive to, ensuring they are from a different class e.g. Pipercillin/Tazobactam plus tobramycin.

Ensure all doses are prescribed as Alder Hey guidelines or BNFc 'severe infection dose' if none available.

If organism(s) are multidrug resistant always discuss options with regional CF team as well as with local microbiology team.

4.6 Long term Pseudomonas aeruginosa growth (IV therapy)

Some patients who chronically grow PsA may require regular IV therapy based on clinical picture. Not all patients will require this and will be based on clinical need by consultant.

4.6.1 Most recent respiratory cultures indicate a growth of Pseudomonas aeruginosa and has had positive clinical response to ceftazidime in the past **and** patient NOT had more than TWO courses of tobramycin in the last 12 months

1st line combination of ceftazidime and tobramycin

Age	1 month – 18 years
Dosage Ceftazidime[13]	IV 50mg/kg max 3g TDS
Dosage Tobramycin[13]	(Only to be initiated once a satisfactory U+E, LFT and FBC has been confirmed) Even if had bloods pre bronchoscopy these need to be repeated when returning to ward (Dose should be prescribed ideally for between 8am to 2pm. This is to aid renal clearance due to better daytime hydration) IV 10mg/kg max 600mg OD (Levels should be taken 20-24 hours post dose on D2 and D7 OR as per local guidelines)

(No more than two courses a year of tobramycin is a guideline to try and prevent hearing loss later on in life. However if clinically necessary patient can have more courses at consultants discretion)

Duration: 14 days

4.6.2 Patient as per 4.6.1 but patient has received **more than two courses** of tobramycin in the last 12 months

To reduce exposure to aminoglycosides substitute colistin (if sensitive) for tobramycin in combination with ceftazidime

Age	Under 60kg	Over 60kg
Dosage Ceftazidime[13]	IV 50mg/kg max 3g TDS	
Dosage Colistin[13]	(Only to be initiated once a satisfactory U+E, LFT and FBC has been confirmed)	
	IV 25,000 units/kg TDS	IV 2,000,000 units TDS

Duration: 14 days

4.6.3 Most recent culture indicated a growth of Pseudomonas aeruginosa and have not responded to initial therapy

Choose a combination of two antimicrobials that the organism(s) are sensitive to, ensuring they are from a different class. Preferably next line antimicrobial should be pipercillin/tazobactam plus another. Meropenem should be reserved for last line therapy to help prevent development of resistance.

Ensure all doses are prescribed as per Alder Hey guidelines or at BNFc 'severe infection dose' if none available

Duration: 14 days (based on clinical improvement)

4.7 Long-term Pseudomonas aeruginosa growth (nebulised therapy)

Those patient who regularly grow Pseudomonas aeruginosa from respiratory cultures despite eradication treatment should receive long term nebulised therapy. This should be continued until respiratory cultures have been clear for 12 months. In those patients who become symptomatic/show declining lung function during this time can also receive two weeks of IV therapy as per 4.6.

4.7.1 Colistin – First line agent

4.7.1a Promixin® – First choice for children over of the age of 2

If child is unable to use the I-Neb Colomycin via EFlow is first line see 4.7.1b

Dosage – Initial test dose required see section 8.1

The I-Neb uses Adaptive Aerosol Delivery technology delivering the dose only on a specific phase of inspiration. This enables the dose of Promixin® via I-Neb to be lower than that when colistimethate sodium is administered via EFlow (below).

Promixin® must be prescribed by its brand name only. For long term use this should be ordered via pharmacy home care department as the most cost effective dispensing route and for ease of delivery to patient.

Age	Dose
>2 years[13]	**1,000,000 units BD (OD at the discretion of consultant)**

Preparation

- 1,000,000 units Promixin® reconstituted with 1 millilitre 0.9% sodium chloride and administered via grey chamber of I-Neb
- **In patients who suffer bronchospasm during test dose** Promixin® vial can be reconstituted with 2.5mg (1ml) of nebulised salbutamol and used immediately.

Duration – As per 4.5.1

[13] BNFc 2020/21 and Alder Hey team clinical experience

4.7.1b Colistimethate sodium (Colomycin®) – First choice for children under of the age of 2 and those who are unable to use the I-Neb

Dosage - Initial test dose required see section 8.1

Age	Dose
<2 years[14]	**1 million units BD**
>2 years[15]	**2 million units BD**

Preparation

- 1 million unit colisimethate sodium reconstituted with 4 mL 0.9% sodium chloride and administered via EFlow through a filter system.
- 2 million unit colisimethate sodium reconstituted with 4 mL 0.9% sodium chloride and administered via EFlow through a filter system.
- **In patients who suffer bronchospasm during test dose** vial can be reconstituted with 2 x 2.5mg (2mL) of nebulised salbutamol and used immediately.

4.7.2 Tobramycin (Tobi® or Bramitob®) Second line

Dosage - Initial test dose required see section 8.1

Please note that these products are only licensed from the age of 6. If being used off license should be under the direction of a consultant.

Usual practice for **prophylaxis** is for 28 days on/off. However, in some patients they may alternate with a second inhaled antimicrobial therapy at the discretion of consultant.

Age	Dose
>6 months[15]	**300mg BD**

Preparation

- EFLow – one vial (Tobi® 300mg/5ml or Bramitob® 300mg/4ml) nebulised accompanied by a filter system.
- I-Neb - **(at the discretion of the CF team)**
  - >12 yrs – 2 fills of lilac chamber
  - <12 yrs – 1 fill of lilac chamber

Duration – As per 4.5.1

[14] BNFc 2020/21
[15] Alder Hey team Clinical experience

4.7.3– Nebulised aztreonam (Cayston®) Third line

Dosage - Initial test dose required see section 8.1

Usual practice for **prophylaxis** is for 28 days on/off. However, in some patients this may be alternated with a second inhaled antimicrobial therapy.

In a select group of patients where other regimes have failed continuous therapy may be required at the discretion of consultant.

Age	Dose
>6 years[16]	**75mg TDS (BD can also be used under direction of consultant)**

Preparation

- EFLow – One 75mg vial reconstituted with one ampoule of 0.17% sodium chloride (included in pack) and nebulised via altera handset (included in the pack) and filter system (not included in pack)
- I-Neb – (**at the discretion of the CF team)** as per EFlow using one lilac chamber fill for BD dosing or one grey chamber fill for TDS dosing

Duration – As per 4.5.1

[16] BNFc 2020/21

4.8 Long term Pseudomonas aeruginosa growth (Dry powder inhalation therapy)

In those patients whom adherence to nebulised therapy is an issue, dry powder delivery may be considered after discussion with regional team.

4.8.1 Colistimethate sodium (Colobreathe®)

Dosage - Initial test dose required see section 8.1

Age	Dose
>6 years[17]	**1.66 megaunit BD**

Preparation

- Administered via specific Turbospin inhaler
- 1.66 megaunits = ONE capsule in inhaler **note that several inhalations may be required to clear inhaler of powder

4.8.2 Tobramycin inhalation powder (Tobi® Podhaler)

Dosage - Initial test dose required see section 8.1

Usual practice for **prophylaxis** is for 28 days on/off. However, in some patients this may alternated with a second inhaled antimicrobial therapy

Age	Dose
>6 years[17]	**112mg BD**

Preparation

- Four capsules (one at a time) to be inhaled via Podhaler device. **note multiple breaths may be required to completely inhale powder

[17] BNFc 2020/21

4.9 Stenotrophomonas maltophilia

4.9.1 Co-trimoxazole

All patients who grow Stenotrophomonas on sputum culture should be discussed with regional CF team. If treatment is required, they should receive Co-trimoxazole (Septrin®).

Due to excellent bioavailability oral treatment is preferred to IV where possible

Contraindications – See BNFc

Monitoring requirements – None for acute course (those who require long term therapy require monthly FBC and LFT monitoring)

Preparations available

- **Liquid**
  - 240mg/5ml
  - 480mg/5ml
- **Tablets**
  - 480mg
  - 960mg

Dose

Age	6 weeks – 5 months	6 months -5 years	6-11 years	>12 years
Dosage ORAL[18]	120mg BD	240mg BD	480mg BD	960mg BD

Age	6 months -5 years	6-11 years	>12 years
Dosage IV	240mg BD	480mg BD	960mg BD

Duration – 14 days

A repeat culture should be taken 14 days after completion to ensure fully treated

4.10 Burkholderia cepacia

All patients who grow B.cepacia should be discussed with regional CF team prior to initialising therapy. Due to high levels of resistance therapy should be based on sensitivities and always discussed with local microbiology team.

[18] Based on dosage in BNFc 2017 and Alder Hey Clinical experience

4.11 MRSA

Refer to section 4.1 (S.aureus). All cases should be discussed with regional team.

Eradication therapy should be attempted twice (see local centre guidelines for therapy choice). If not effective IV therapy is preferred (see local centre guidelines for therapy choice)

5. Fungal infections

5.1 Aspergillus fumigatus

Consider treatment in any patient who regularly cultures aspergillus on cough swab or if had more than one episode of ABPA particularly those with serological evidence of infection.

5.1.1 Acute treatment

5.1.1.1 Liposomal amphotericin (Ambisome®)

Age	All ages	Notes
Dosage[19]	**At start of all courses IV 0.1mg/kg (max 1mg) test dose with observations 30 minutes post completion** **THEN** **IV 3mg/kg OD (if severe infection 5mg/kg OD should be used with close monitoring of FBC and LFT)**	**Two preparations are available of amphotericin care should be taken and prescribed by brand only** **Base line FBC, LFT and UE should be taken and repeated at D2, 5 and D10**

[19] CF trust antimicrobial guidelines

5.1.2 Long term treatment

5.1.2.1 Itraconazole – First line

Preparations available –

- 10mg/ml liquid ***preferred due to better absorption**
- 100mg capsules

Contraindications – See BNFc

Monitoring requirement -

- **This interacts with modulator therapies and lead pharmacist must be consulted prior to starting**
- Itraconazole levels should be taken 4 hours **post dose** after a minimum of 2 weeks of therapy. Levels should then be checked regularly throughout treatment, particularly if a patient's renal function is reduced or LFT's are raised.
- Additionally if patients switch to capsules, levels should be taken after 2 weeks to see if absorption is being affected

Levels should be between 5-15 mg/L (contact pharmacy for further advice)

- LFT's and renal function need to be checked prior to commencing Itraconazole and regularly throughout treatment based on clinical history. Speak to pharmacy for further guidance.

Dosage

Age	All ages	Notes
Dosage[20]	**2.5mg/kg BD Max 200mg BD (initial dose)**	**Total daily dose can be administered in a single dose. Should be taken on an empty stomach to further aid absorption. Dose adjusted per levels**

Duration – based on clinical effectiveness and at consultants discretion

[20] BNFC 2020/21

5.1.2.2 Voriconazole – Second line (after discussion with regional CF team)

In those patients who do not tolerate itraconazole or if there is persistent growth of aspergillus in cultures, consider switching to voriconazole.

Special considerations

Voriconazole is associated with a risk of phototoxicity, skin squamous cell carcinoma (SCC) and liver toxicity. It is therefore important to adhere to the advice on phototoxic reactions, monitoring for SCC and liver toxicity given in the product information. Prescribers must complete the Health Care Professional checklist when treatment is initiated or reviewed, counsel the patient on the risks and give them the alert card.

(http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON418519)

Contraindications – See BNFc

Preparations available –

- 200mg/5ml liquid **for under 12s**
- 50mg tablet **for over 12s**
- 200mg tablet **for over 12s**

Monitoring requirement –

This interacts with modulator therapies and lead pharmacist must be consulted prior to starting

Voriconazole levels should be done at least once in all patients **but always in those with acute infection**.

- Measure an initial pre dose level on day 4 or 5.
- The serum sample must be taken immediately pre-dose.
- Your local lab may have to send samples off to national centre for testing so time taken to receive levels may be longer than usual.
- The usual therapeutic range for the serum level of voriconazole is 1.3 to 5.7mg/L.
- Levels should be repeated 4 or 5 days after any change in the dose of voriconazole and for stable patients, levels should be repeated every 4 weeks unless the clinical situation demands otherwise.

Dosage[21] (tablet and liquid dosage forms are not bioequivalent)

Age	Under 12	Over 12	
		<40kg	>40kg
Loading dose For 24 hours	IV 9mg/kg 12hrly (two doses only) Oral not recommended	IV 6mg/kg 12hrly Oral 200mg 12hrly	IV 6mg/kg 12hrly Oral 400mg 12hrly
Maintenance dose	IV 8mg/kg BD Oral 9mg/kg (max 350mg) BD liquid	IV 4mg/kg 12hrly Oral 100mg 12hrly tablets	IV 4mg/kg 12hrly Oral 200mg 12hrly tablets

[21] BNFc 2020/21 and Alder Hey Oncology infection guidelines

5.1.2.3 Posaconazole – Third line

Posaconazole oral suspension should be taken with food (preferably a high fat meal) or nutritional supplement to ensure adequate exposure for systemic effects. Where possible, tablets should be used in preference to suspension because tablets have a higher bioavailability.

Posaconazole oral suspension is not interchangeable with tablets on a milligram-for-milligram basis.

This interacts with modulator therapies and lead pharmacist must be consulted prior to starting

Dosage (tablet and liquid dosage forms are not bioequivalent)

Contraindications – see BNFc

There is a lack of evidence for use in children and all doses are based on adult data.

Preparations –

- Liquid - 40mg/ml
- Tablets - 100mg tablets

Age	>12s
Dosage[22] Suspension	400mg BD
Dosage Tablets	300mg BD for first day THEN 300mg OD
Can be used in younger children after discussion with lead pharmacist	

[22] BNFc 2020/21

5.1.4 Nebulised amphotericin – Fourth line

In those patient who are not able to take oral treatment, nebulised amphotericin is an option once a MDT meeting at the regional centre has taken place. It should be noted that this is an unlicensed route for preparations that are currently available on the market.

Preparations available – See below

Monitoring requirement - Administration of a bronchodilator is advised prior to dose. Bronchospasm can occur in patients receiving amphotericin. If this occurs treatment options should be discussed with MDT.

Dosage - Initial test dose required see section 8.1

Age	All ages	Notes
Dosage[23]	**25mg BD**	**To be administered via conventional compressor & AeroEclipse device** **Two preparations are available Fungizone and Ambisone** • **Fungizone® (First line due to cost) - Reconstitute one 50mg vial with 8ml WFI and nebulise 4ml as above** • **Ambisome® (second line due to high cost) to be used if Fungizone is not tolerated – Reconstitute one 50mg vial with 12ml WFI and nebulise 6ml as above (when drawing up 6ml ensure filters included with Ambisome® are used)**

5.2 Exophiala

All cases should be discussed with microbiology team for advice. **Doses for commonly used medications can be found in this document.**

[23] CF trust antimicrobial guidelines

6. Fungal prophylaxis whilst on IV therapy

Treatment with nystatin is advised whilst on IV antimicrobial therapy and for one week after to prevent fungal growth.

Monitoring requirements – None for acute course

Preparations available –

- **Liquid**
  - 100,000 unit/ml
- **Tablets**
  - 500,000 unit/tablet

Dose

Age	<1 year	1 year – 12 years	>12 years
Dosage[24]	**100,000 units QDS**	**250,000 units QDS OR 500,000 units BD**	**500,000 units QDS**

Duration – whilst on IVs and one week post completion

[24] Alder Hey team Clinical experience

7. Mycobacterium species

It is important that the sub group is established prior to starting therapy

7.1 Mycobacterium abscessus

Infection with Mycobacterium abscessus is more likely to result in progressive lung disease. **All cases should be discussed with regional CF lead.** Microbiological cure is unlikely and treatment is aimed at improving clinical wellbeing.

Treatment as set out by the CFF/ECFS/BTS guidelines should be followed[25]. Medications listed below can be substituted as per regional CF lead after discussion with ID/microbiology. This will be due to age of patient and licensing of medication.

If medication to be used is not included in this document the 'severe infection' dose should be used

All medications have potential to affect blood count, liver function and kidney function. Close monitoring of all is advised weekly during initiation (IV) phase and monthly during continuation phase

7.1.1 Imipenem

Age	All ages	Notes
Dosage	25mg/kg (max 1g) Every 6 hours	• Product is Imipenem-Cilastatin Sodium 250mg/250mg or 500mg/500mg • Dose stated is of Imipenem content only • Under certain circumstances total daily dose can be given BD after discussion with senior pharmacist • Can cause severe nausea and vomiting. Strongly advise co-prescribing antiemetic to be administered pre dose see below

7.1.2 Tigecycline

Age	8-12 years	>12 years	Notes
Dosage	1.2mg/kg BD (Max 50mg BD)	100mg loading dose followed by 50mg BD	• Can cause severe nausea and vomiting. Strongly advise co-prescribing antiemetic to be administered pre dose see below • Can be used from the age of 6 at 1.2mg/kg BD after discussion with senior pharmacist and lead consultant

[25] http://thorax.bmj.com/content/71/Suppl_1/i1

7.1.3 Amikacin

<table>
<tr><th>Age</th><th colspan="2">All ages</th><th>Notes</th></tr>
<tr><td>Dosage
IV for initiation phase</td><td colspan="2">30mg/kg OD</td><td>Discuss with audiology before starting if clinically suitable
Therapeutic drug monitoring required around second dose.
• Trough levels <2mg/L
• <u>Only under instruction of a senior pharmacist</u> - Peak level of 20–50 mg/L
Further levels to be taken as per local guidelines however at least on D2,7 and 10
(Dose should be prescribed <u>ideally</u> for between 8am to 2pm. This is to aid renal clearance due to better daytime hydration)</td></tr>
<tr><td rowspan="2">Dosage
Nebulised for continuation phase</td><td>6-12 yrs</td><td>>12 years</td><td rowspan="2">Administered via Ombra compressor and aeroeclipse with filter.
Prepared as follows:
• 250mg - 1ml of 250mg/ml IV solution mixed with 3ml Sodium Chloride 0.9%
• 500mg - 2ml of 250mg/ml IV solution mixed with 2ml Sodium Chloride 0.9%

(other nebuliser devices can be used ONLY under supervision of network physiotherapist)

Can be used under the age of 6 only after discussion with network lead pharmacist</td></tr>
<tr><td>250mg BD</td><td>500mg BD</td></tr>
</table>

7.1.4 Cefoxitin

Age	All ages	Notes
Dosage	**40mg/kg QDS (max 3g) by IV bolus over 5 minutes**	**Unlicensed import. Please ensure pharmacy department given advanced notice of need to ensure sufficient stock is available for treatment.**

7.1.5 Azithromycin (see 3.1.3)

Note – If cultures show resistance do not use

*favoured over clarithromycin due to reduced chance of interactions and reduced chance of resistance.

7.1.6 Clofazimine

Preparations available:

Please note preparations are hard to obtain and most likely will be imports. Supply will most likely need to come from hospital and will take time to get stock.

- Liquid – none available
- Capsules
    - 50mg soft capsules
    - 100mg soft capsules

Age	All ages	Notes
Dosage	**1-2mg/kg OD (max 100mg)**	**Dose as tolerated** **Note lack of available dosage forms. Dosage should be rounded accordingly**

7.1.7 Minocycline

Note – Not recommended in young children due to long term effects on bones and teeth. Consider discussion with microbiology for alternative agent or frank discussion around possible side effects.

Preparations available

- Liquid
    - None available
- Tablet
    - 50mg (NOT MR)

Age	All ages	Notes
Dosage	**2mg/kg OD (max 200mg)**	**This dose is not for general infections**

7.1.8 Moxifloxacin

Preparations available

- Liquid
  - None available
- Tablet
  - 400mg

Age	All ages	Notes
Dosage	**10mg/kg OD (max 400mg)**	**No liquid preparation is available round to nearest 100mg and disperse a proportion of tablet in water e.g. ¼ tablet in water for 100mg dose.** **Manufacturer confirms uniform dispersion throughout dosage form so accurate dosing can be achieved.**

7.1.9 Linezolid

Preparations available

- Liquid
  - 100mg/5ml
- Tablet
  - 600mg (can be halved)

Age	1 month – 11 years	12+ years
Dosage	**10mg/kg TDS (max 600mg)**	**600mg BD**
Should have baseline eye examination prior to starting and warned to report issues with changes in vision urgently to team **Avoid tyramine rich foods whilst taking (seek dietician advice)** **Base line FBC and LFT should be taken and checked weekly for first month of treatment followed by monthly**		

7.1.10 Co-trimoxazole

See 4.9.1

7.1.11 Antiemetics whilst on treatment

The medications used as part of this regime are known to cause severe nausea and vomiting. Therefore to prevent these symptoms early intervention with antiemetics is essential particularly during the induction phase. Early consideration of TPN should be discussed with the dieticians to prevent severe weight loss.

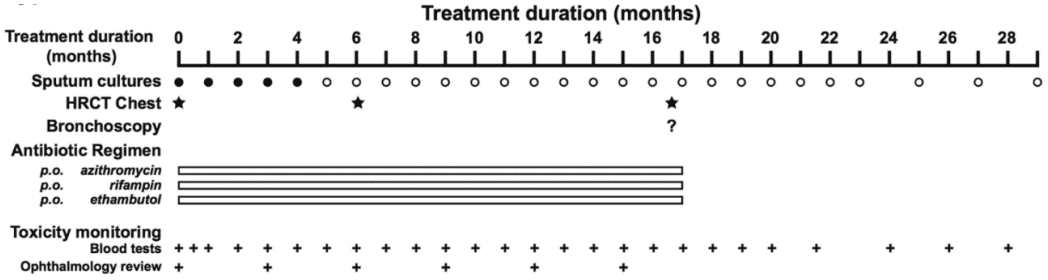
- **IV** ondansetron 0.15mg/kg (max 6mg) TDS should be prescribed regularly from the start of treatment.
- If this is not effective levomepromazine should be administered **IV in addition** to the ondansetron at a dose of 0.1-0.2mg/kg OD-BD (max 25mg).
- If patient continues to suffer from nausea/vomiting despite maximal dosing the levomepromazine can be **replaced** by oral aprepitant as per BNFc (note that this can continue for multiple days if needed). **This interacts with modulator therapies and lead pharmacist must be consulted prior to starting**
- On discharge patient should receive oral ondansetron 0.1mg/kg (max 4mg) PRN/TDS.

7.2 Mycobactium avium complex

Patients should receive triple therapy with a macrolide, rifampicin and ethambutol. Therapy should continue until sputum cultures are clear for 12 months and confirmed by culture.

Treatment as set out by the CFF/ECFS/BTS guidelines should be followed[26].

All medications have potential to affect blood count, liver function and kidney function. Close monitoring of all is advised



7.2.1 Azithromycin (see above for dosage)

7.2.2 Rifampicin

Preparations available

- Liquid
  - 100mg/5ml
- Capsules
  - 150mg
  - 300mg

Age	All ages	Notes
Dosage	**15mg/kg OD (max 600mg)**	• **Has multiple interactions with other medications. Check with pharmacist before prescribing**

This interacts with modulator therapies. Lead pharmacist must be consulted before starting

[26] http://thorax.bmj.com/content/71/Suppl_1/i1

7.2.3 Ethambutol

Preparations available:

- Liquid
  - Extemporaneous preparation 100mg/ml
- Tablets (if dose rounded can be crushed and mixed with water)
  - 100mg
  - 400mg

Age	All ages	Notes
Dosage	**15mg/kg OD**	• **Ethambutol should be used with caution in children until they are at least 5 years old and capable of reporting symptomatic visual changes accurately.** • **Routine eye tests are not required** • **Renal function should be checked before treatment.** • **Visual acuity should be tested by Snellen chart before treatment with ethambutol.**

8. Appendix

8.1 Inhaled antimicrobials initial test dose

DRUG RESPONSE ASSESSMENT TESTING PROFORMA

*******THE TEST WILL NOT BE UNDERTAKEN WITHOUT ALL SHADED AREAS COMPLETED******

APPROPRIATE PRESCRIPTION ATTACHED? ☐

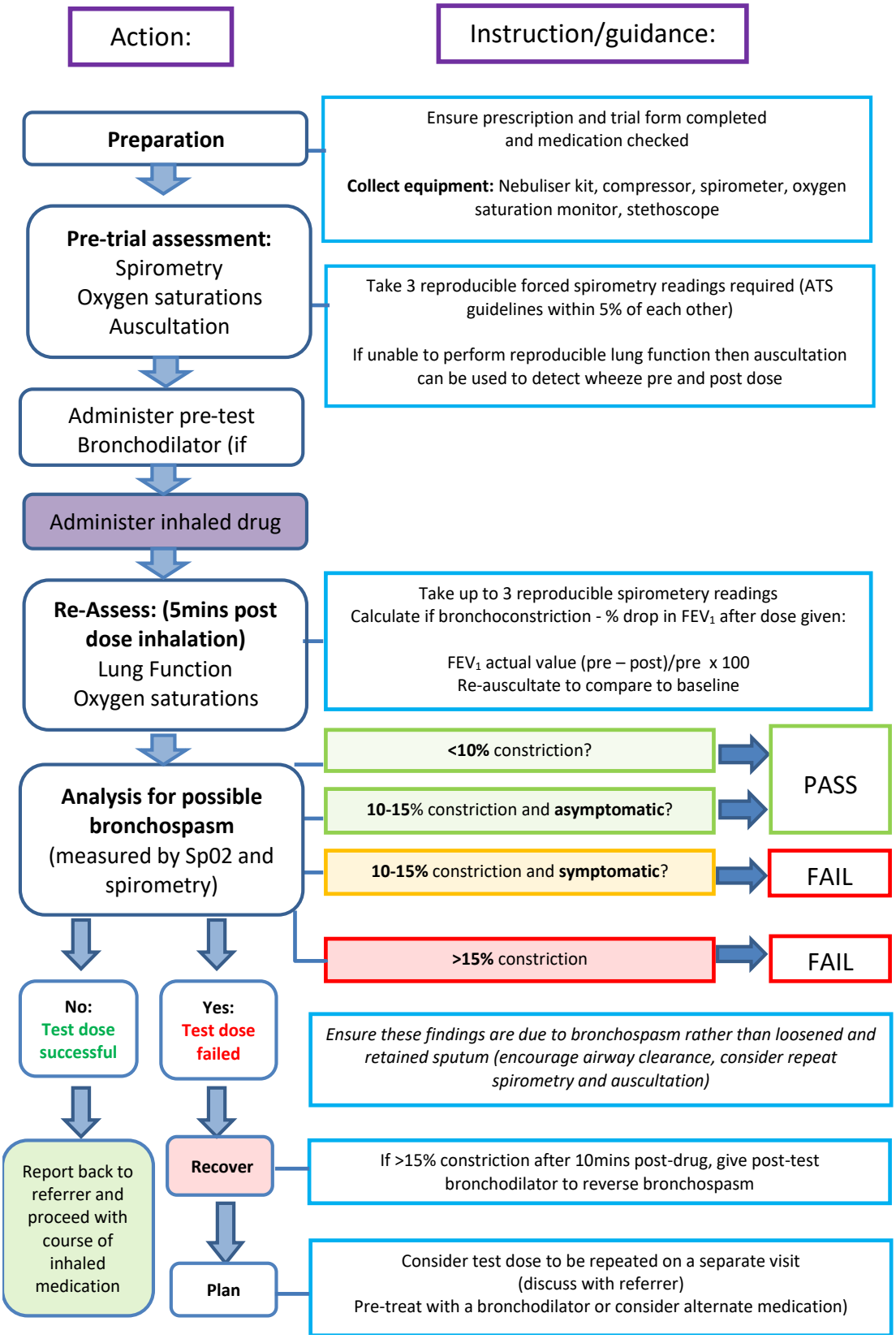
PATIENT NAME: **DOB:** **HOSPITAL NO:**	**Inpatient/ Outpatient**
DATE OF TRIAL: **REASON FOR REFERRAL:** **PRESCRIBER:** **HCP carrying out DRA:** **CONSULTANT:**	**ALLERGIES**

	Medicine	DOSE	Administered?
MEDICATION FOR TEST DOSE			**YES NO**
Diluent (e.g. 0.9% saline for Colistin/Amikacin etc)			
PRE TEST BRONCHODILATOR *(if required)*			**YES NO**
POST TEST BRONCHODILATOR *(if required)*	**Salbutamol NEB** **INHALER**	**……mg** **……puffs**	**YES NO**

Equipment to be used	Conventional	i-neb	e-flow Conventional
DPI/Nebuliser	Sidestream/Pari LC plus/Other	Green/Grey/Lilac	Normal/Altura

	FEV_1	Sp02	Other (e.g. ausc/HR)
PRE test	**L/min**		
POST test	**L/min**		
% change	*(see guidance attached)*		
Symptoms/ comments			
10 mins post *(if needed)*	**L/min %** **pred.**		
% change			
Symptoms/ comments			

Explained potential side effects	Y/N	Patient Information leaflet	Y/N
Inhalation technique discussed	Y/N	Pharmacy notified/form completed	Y/N
Equipment explained	Y/N	Patient aware how to access repeat prescription	Y/N
Plan	4-6 week review agreed: Y/N Phone/Email/clinic/telehealth		


Action:
Instruction/guidance:
Preparation
Ensure prescription and trial form completed and medication checked
Collect equipment: Nebuliser kit, compressor, spirometer, oxygen saturation monitor, stethoscope
Pre-trial assessment:
Spirometry
Oxygen saturations
Auscultation
Take 3 reproducible forced spirometry readings required (ATS guidelines within 5% of each other)
If unable to perform reproducible lung function then auscultation can be used to detect wheeze pre and post dose
Administer pre-test Bronchodilator (if
Administer inhaled drug
Re-Assess: (5mins post dose inhalation)
Lung Function
Oxygen saturations
Take up to 3 reproducible spirometery readings
Calculate if bronchoconstriction - % drop in FEV1 after dose given:
FEV1 actual value (pre – post)/pre x 100
Re-auscultate to compare to baseline
Analysis for possible bronchospasm
(measured by Sp02 and spirometry)
<10% constriction?
10-15% constriction and asymptomatic?
PASS
10-15% constriction and symptomatic?
FAIL
>15% constriction
FAIL
No:
Test dose successful
Yes:
Test dose failed
Ensure these findings are due to bronchospasm rather than loosened and retained sputum (encourage airway clearance, consider repeat spirometry and auscultation)
Report back to referrer and proceed with course of inhaled medication
Recover
If >15% constriction after 10mins post-drug, give post-test bronchodilator to reverse bronchospasm
Plan
Consider test dose to be repeated on a separate visit (discuss with referrer)
Pre-treat with a bronchodilator or consider alternate medication)

CF Antimicrobial Guidelines	
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Ratified by:	Medicines Management and Optimisation Committee (MMOC)
Date ratified:	16th May 2022 (ag)
Name of originator/author:	Andrew Lilley (Clinical Pharmacy Services Manager / Lead Pharmacist - Respiratory)
Name of responsible group:	Respiratory Team
Date issued:	24th May 2022
Review date:	16th May 2025

Version Control Table				
Version	Date	Author(s)	Status	Comment(s)
3	May 22	A Lilley and R Rowley (Pharmacist)	Current	
2	Jan 20	A Lilley	Archived	
1	Nov 17	A Lilley	Archived	

Review and Revision(s) Log *Record of revision(s) made to guidelines since Version 2*			
Section Number	Page Number	Revision(s) made	Reason for revision(s)
2.1.1	6	Statement on those on old prophylaxis regimen	For clarification
4.7.3	20	Chamber type altered	Based off experience
5.1.2.1/2/3	25-27	Statement on interaction with modulators	For safety
7.1.3	30	Statement on nebuliser device and off license usage	Based off experience
7.1.3	30	Comment on need for audiology referral	Based off new guidelines from audiology
7.1.11	34	Ondansetron dose amended based of experience with patients	For clarification
7.1.11	34	Extra information regarding length of use of aprepitant	For clarification
7.2.2	35	Statement on interaction with modulators	For safety