GUIDELINES / STANDARDS FOR THE MANAGEMENT OF CHILDREN & YOUNG PEOPLE WITH CYSTIC FIBROSIS

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Key Amendments

Date	Amendment	Approved by
August 2013	New Guideline	
September 2015	Document extended for 12 months as per TMC paper approved on 22nd July 2015	TMC
January 2016	Amendments made to reflect the new CF service and updates of treatments, physiotherapy and Ivacaftor	
October 2020	Document Revised	
19th Nov 2020	Document extended for 1 year	Dr J West/ Paediatric QIM
March 2021	Document Revised – amendments to guidance on oral treatment antibiotics, tobramycin levels, vitamin prescription and exposure to varicella in CF Inclusion of section on new precision medications	
19th May 2021	Documents reviewed and approved for 3 years	Paediatric QIM
14th July 2021	Document reviewed and ratified	Medicines Safety Committee
9th Feb 2023	Document reviewed, staffing details, sections on modulators, vitamins and hearing testing updated	Paediatric Guideline Review Day

Introduction

Cystic fibrosis is an autosomal recessive genetic disorder that affects the lungs, pancreas, liver, and intestine. It is characterised by abnormal transport of chloride and sodium across an epithelium, leading to thick, viscous secretions. Chest exacerbations need to be recognized and treated promptly. Higher doses and longer antibiotic courses are required than for people without CF. This guideline covers medical treatments for children and young people with cystic fibrosis as well as guidance for inpatient and outpatient attendances.

This guideline is for use by the following staff groups:

Medical and nursing staff

Lead Clinician(s)

Dr Clare Onyon	Consultant Paediatrician
Dr Paul Watson	Consultant Paediatrician
Nicki Wedgbury	CF Specialist Nurse
Alex Macdonald	CF Specialist Nurse
Jo Colley	CF Specialist Physiotherapist
Cathy Pollard	CF Specialist Dietitian
Amy Symonds	Clinical Psychologist

CONTENTS

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Cathy Pollard CF Dietitian	 EXT: 33694
Clinical Psychologist Dr Amy Symonds	 07525 906557

Team Mobile (only on during working hours) 07775 682570

Out of Working Hours Contact

All CF patients have indefinite open access to Riverbank Ward, where advice can be sought either in person or by telephone. If more specific CF advice is needed, staff from Riverbank Ward can contact the CF team either within the hospital (Dr Onyon is happy to be contacted via switchboard), or at BCH if local team not available.

A member of the local CF team should be informed of any contact with a CF patient so that they can be followed up as appropriate

2 Inpatient services

2.1 Reason for admission

Children are usually admitted for intravenous antibiotics:

- Because of chest exacerbation
- Because of marked weight loss (+/- supplemental feeding)
- As part of a 'regular' antibiotic regime
- In preparation for an operation under general anaesthetic

Occasionally inpatient management may be required to establish treatment at the time of diagnosis, for meconium ileus equivalent (MIE/DIOS), intractable feeding problems or a rarer complication of CF.

2.2 Admission procedure to Riverbank Ward, Worcestershire Royal Hospital

a) CF patients to be admitted to a cubicle with separate toilet facilities
b) Clerk and examine (use admission sticker – see appendix 1)
c) Baseline weight, height and saturations
d) Write up drug chart before parents leave and check availability of medications
e) Check latest sputum culture (usually from last clinic visit) and antibiotic sensitivities.
f) Check need for annual bloods (if not done in the last year, or if indicated in outpatient entry).
g) Specific aspects of management or investigations, as described by doctor arranging admission check last outpatient entry.
h) Insert cannula or long line (Vascuport needles can be inserted by some ward nurses or CF specialist nurses). If long line needed apply local anaesthetic cream to chosen sites (not all patients require a long line- some may prefer a cannula, discuss with team). Use of filter to be discussed with CF team. Heparin should not be used for long lines or cannulas.
i) Inform dietitian and physiotherapy of admission. Physiotherapy is usually twice daily and dietitian review twice weekly.
j) Lung function is usually done at the beginning, middle and end of intravenous antibiotic courses. This may be organised remotely by the CF team for those patients with their own devices.
k) Overnight saturations monitoring for first night
l) Sputum or cough plate /swab carried out with lung function at beginning, middle and end of admission.
m) 3 post meal blood sugars to be done an hour after food (within 24-48 hours)
n) MRSA swabs should be considered on admission
o) Review on the ward is usually at least twice a week by the CF consultant, and every working day by a member of the CF team if team are working onsite.
p) TOBRAMYCIN LEVELS. Once daily regime trough levels pre second dose (preferably immediately before dose due) (not via Vascuport or percutaneous longline) and then weekly. Aim for: pre dose level: <1mg/l. If levels are high reduce dose by 10%. Repeat levels the following day pre dose.
q) Colomycin nebulisers should be given to all CF patients on admission regardless of pseudomonas status (IF USUAL NEBULISER IS BRAMITOB [TOBRAMYCIN] CHANGE NEBULISER TO COLOMYCIN DURING ADMISSION WHILST ON IV TOBRAMYCIN)

In the event of 2 patients with CF being on the ward at the same time, different nurses should be allocated to each patient. Ideally patients should be placed on opposite sides of the ward.

Whilst on the ward, CF patients are allowed to visit all communal areas. If another CF patient or patient with pseudomonas or other infective respiratory pathology is on the ward, they must not be in contact.

3 Clinic

3.1 Outpatient Services

Clinics are mainly run on a Thursday morning or Friday alternating between the Alexandra Hospital and Worcestershire Royal Hospital in Children's clinic. All members of the CF team will be available.

3 Clinics per year will be shared clinics with members of the CF team from Birmingham Children's'

Hospital.

Patients over the age of 1 year are usually seen every 2 months. Some patients alternate their visits with the BCH team; some are seen for two visits in Worcestershire to each visit at BCH. Patients under 1 year are seen at least once a month, usually alternating with BCH.

- Patients are to come straight to their designated clinic room on arrival and members of the CF team will come to them to avoid close contact with other patients in the waiting areas.
- All equipment is cleaned between each patient.
- Height, weight and oxygen saturations should be measured at each clinic visit
- All patients to have cough / swab or sputum sent at each visit
- Random glucose test to be measured if taking corticosteroids or weight loss
- Patients to have lung function at each visit from reception age.
- Psychosocial needs will be assessed at clinic appointments
- During the transition period, patients are offered to attend part of the appointment without their parents being present
- Urgent clinic review is available and separate clinic slots are available for patients with MRSA and burkholderia cepacia
- Serious clinical problems are communicated to BCH within 5 days of the clinic appointment

Video appointments

During the COVID pandemic a number of clinic appointments have been virtual video appointments. Appointments will continue to be a mixture of face to face and virtual clinics. For a virtual appointment cough swabs are done at home and dropped in to the patient's GP surgery. Height and weight can be done at home or during other attendances to hospital (for example when having bloods taken), lung function will also be done with home monitoring devices where applicable. The child or young person should be available for virtual appointments.

3.2 Additional Outpatient appointments

Nebuliser trials

- First administration of DNase (Appendix 2 & 3), Hypertonic saline (Appendix 4 & 5) and Colomycin (Appendix 6 &7) must be observed in clinic to ensure there are no adverse reactions. Details of nebuliser trials need to be sent (via email) to BCH physio team and pharmacist with following letter to BCH team.

- Lung function should be done before and after administration of these medications where possible to ensure no bronchoconstriction.
  One month's supply of DNase is usually prescribed at this initial appointment. Assessment of response to DNase is usually made at 1 month with clinic review and lung function. After review of DNase at one month, home delivery can be arranged by BCH.

- Nebuliser compressor units (most commonly Pari-Turbo boy) will be supplied by the CF team. Presently there is no servicing contract therefore units will need to be replaced when faulty. Filters need changing yearly; we ask that patients bring these in with annual bloods.

- A small number of E-flow nebuliser units are available for those patients that require multiple nebulised medication to reduce treatment time. This will be decided on an individual patient basis. The e-flow heads need changing every 6 months and will be provided by the CF team.

4 Home and Community Visits

Home visits offer families the undivided attention of a health professional away from a busy ward or clinic in the security and privacy of their own home. This provides the opportunity for less hurried discussions about anything the family wish to talk about. In particular, practical issues can be dealt with and it gives us an opportunity to explore how the family is coping with the situation of living with a child with CF. Home visits can be an ideal opportunity to involve both parents, the child, siblings and extended family members.

In order to maximise the effectiveness of visits, appointments are made with the family responding to their individual needs regarding frequency and content. The team will endeavour to make appointments at a time convenient to the family and school aged children can be seen before or after school. Additional contact, support, and follow up are also maintained by telephone on a two-way basis. Home visits should not be allowed to be a substitute for regular clinic attendance.

The service will provide specialist CF care at home and in the community. The purpose of visits may involve:

- Monitoring and assessment including measurement of SpO2, lung function and collection of specimen e.g. sputum, cough swabs.
- Education on inhaled medication use and regimens
- Education, reinforcement and encouragement following:
    - diagnosis
    - commencing shared care service
    - diagnosis of new complication
    - commencement of new treatments
    - preparation for transition
- Nursery, pre-school and school visits to provide education to staff and carers, to provide a care plan for the establishment and address any issues affecting CF care and education.
- Flush portacaths / change portacath needles (nurses only)
- Assessment and review of airway clearance techniques advice on exercise, posture correction and stress urinary incontinence (physio only)
- Support including specific psychological support for children and/or parents

5 Medication

ANTIBIOTICS

Chest exacerbations need to be recognized and treated promptly. Higher doses and longer antibiotic courses (both oral and intravenous) are required compared to people without CF.
If patients on prophylactic antibiotics are started on a treatment course of antibiotics these are normally discontinued and restarted once the treatment course has been completed.
Children are rarely given oral antibiotics during admission but should resume their usual prophylactic oral antibiotics on discharge.

5.1 ORAL TREATMENT ANTIBIOTICS usually 2-3 week course

Treatment	Age/weight/	Dose	Frequency	Max per dose^
Amoxicillin (usually given with flucloxacillin)	1mth-18yrs	25-50mg/kg **or** 30mg/kg	BD TDS	2g BD 1g TDS
Azithromycin*	6mths-18yrs	10mg/kg	OD	500mg daily
Ciprofloxacin**	1mth –18yrs	20mg/kg	BD	750mg BD
Clindamycin (for staph aureus)	1mth-18yrs	5-7mg/kg	QDS	600mg QDS
Co-amoxiclav (Amoxicillin/ clavulanic acid)	1mth-18yrs	25mg/kg	BD	Max 1g amoxicillin BD. Max125mg clavulanic acid / dose Use 400/57 suspension **Or** 500/125 tablets (can add extra 250mg or 500mg amoxicillin tablet BD to make up 25mg/kg dose in addition to co-amoxiclav – see dosage table below #)
	>12 years	**Or** 250/125 or 500/125 tablets	TDS	500mg /125mgTDS
Flucloxacillin	1mth-18yrs	25-50mg/kg **or** 30-35mg/kg	BD TDS	Total daily dose 100mg/kg or 4g/day

* Give for a 2 week course in the first instance (other antibiotics are usually given for 3 weeks)

** Ciprofloxacin should not be commenced without consultant discussion. Ciprofloxacin should only be prescribed when other recommended antibiotics have failed or will not work due to resistance (MHRA alert Jan 2024)

Use preparation with lowest clavulanic acid content i.e. for dose of 1g amoxicillin use 1x625mg Co-amoxiclav and 1x500mg Amoxicillin. Ensure not to exceed usual clavulanic acid dose using BNF-C dosing.

Co-amoxiclav treatment dosing table

Patients Weight	Co-amoxiclav	Amoxicillin	Frequency	Total amoxicillin per dose
20-25kg	1 x 500/125	0	BD	500mg
26-35kg	1 x 500/125	1 x 250mg	BD	750mg
36-40kg	1 x 500/125	1 x 500mg	BD	1000mg

5.2 Specific antibiotic regimes

Newly diagnosed CF with chest infection (no pathogens)

a) IV CO-AMOXICLAV for 2 weeks, then:
b) Oral AMOXICILLIN and FLUCLOXACILLIN (or AUGMENTIN) for 3-4 weeks then:
c)

If <1 year old: ~ continue FLUCLOXACILLIN until 12-24 months, add 3 week courses AMOXICILLIN for coughs
If >2 year: give 3 week courses AMOXICILLIN & FLUCLOXACILLIN for coughs

NB If allergic to penicillin, please discuss with CF team and consider referral to the Worcestershire Allergy team for delabelling / challenges

First and second isolation of *Pseudomonas aeruginosa* from sputum/cough swab:

If asymptomatic:

i) Oral CIPROFLOXACIN for 4 weeks, and
ii) Nebulised COLOMYCIN for at least 3 months (*stop after 3 clear cough swabs which will be organised by the respiratory nurses*.)

Follow up 1 month later for further cough swab off treatment.

If symptomatic:

i) IV TOBRAMYCIN and CEFTAZIDIME (according to sensitivities) for 2 weeks, and
ii) Start and continue nebulised COLOMYCIN *for at least 3 months (may stop after 3 clear cough swabs)*.

Follow up 1 month later for further cough swab off treatment.

Other antibiotics

Oral Clarithromycin, moxifloxacin, nebulised amikacin or meropenem may be used in the case of Mycobacterium abscessus infection

5.3 Antibiotic prophylaxis - indicated for some children

Antibiotic	Comments	Age/weight	Dose	Frequency	Availability
Flucloxacillin	Prophylaxis (usually under 2-3 years but can be used in older children) Co-amoxiclav duo may be used if not tolerated.	< 3 years > 3 years	125mg 250mg (some non-trial patients on 25mg/kg)	BD	Cap 250mg, 500mg Syrup 125mg/5ml 250mg/5ml
Co-trimoxazole	Prophylaxis	> 2/3 years	24mg/kg	BD	Tab 480mg

			(max 960mg/dose)		Susp 240mg/5ml, 480mg/5ml
Azithromycin	Used if other problems, severe lung disease, or don't tolerate other antibiotics Has anti-inflammatory effect	6months – 18yrs	10mg/kg (max 500mg/dose)	OD on M/W/F	Cap/tab; 250mg Susp; 200mg/5ml
Doxycycline	Prophylaxis for teenagers *Watch for photo-sensitivity*	**>12 years only**	100-200mg (max 200mg per dose)	OD	Cap; 50mg, 100mg Disp Tab; 100mg

5.4 Intravenous antibiotics

An IV antibiotic regime may be suggested in the latest outpatient entry. Otherwise stop
Oral antibiotics and give first line regime, heeding any past allergic reactions and current sputum sensitivities.
Courses usually last 2 weeks

First line regime:

Sputum culture	Antibiotics
Pseudomonas aeruginosa	Tobramycin + Ceftazidime
Never isolated *Pseudomonas aeruginosa*	Co-amoxiclav

IV antibiotic doses:

Antibiotics	**Age/weight**	**Dose (per kg)**	**Frequency**	**Max**	**Therapeutic Drug Monitoring**
Ceftazidime	1mth-18yrs	50mg/kg	TDS	Max 3g per dose	N/A
Co-amoxiclav	1mth-18yrs	30mg/kg	TDS	Max 1.2g per dose	N/A
Meropenem	1mth-18yrs	40mg/kg	TDS	Max 2g per dose	N/A
Tobramycin *Levels needed before 2nd dose* *Ensure not on nebulised tobramycin (Bramitob)at the same time*	1mth- 18yrs	10 mg/kg* *Use ideal weight for height in obese patients*	OD	Max 660mg per dose	Levels pre-2nd dose then weekly (See below)

Tazocin (Piperacillin with tazobactam) - *Second line Antipseudomonal Note contains penicillin*	1mth-18yrs	90mg/kg	QDS	max 4.5g per dose	N/A
Amikacin # Following discussion with BCH CF team *Levels needed before 3rd dose*	1mth- 12yrs	15 mg/kg	OD	Max 1500mg	Levels pre-3rd dose then weekly

*preferably use the dose which most recently gave satisfactory levels

Rarely given for non-tuberculosis mycobacteria (NTM) or more resistant Gram-negative bacteria – to be discussed with BCH CF team

5.5 Administration and monitoring levels

- Tobramycin is given once daily and is made up dose to 30 ml with 0.9 % saline and infuse via pump over 30 minutes
- Round up the antibiotic dose to a sensible value and try to use whole vials especially with Ceftazidime (this does not apply to tobramycin or amikacin where the dose is decided by levels)

Aminoglycosides like tobramycin are at risk of causing ototoxicity or auditory dysfunction. This risk is increased with dehydration and concomitant use of neurotoxic drugs. Patients should be counselled of the risk and clear documentation in the notes this has been explained (on the CF admission sticker).

Monitor patients on aminoglycosides for auditory dysfunction (including tinnitus) as they can cause ototoxicity. Audiology is recommended following a course of IV tobramycin, particularly if the has been raised trough level, for all patients starting on amikacin and every 1-2 years if on regular IVs containing aminoglycosides. Any auditory disturbance should be reported and treatment reviewed promptly.

TOBRAMYCIN LEVELS.
Timing: Pre-second dose (trough) – maximum 1 hour pre-dose, preferably immediately before dose due. Levels should be taken and dose given.
NB: Do not take levels from vascuport or percutaneous longline

Aim: Pre dose level <1mg/L

If levels are >1mg/L:

1. Stop Tobramycin
2. Repeat level after 24 hours
3. Once <1mg/L, restart Tobramycin at a reduced dose of 10-20%
4. After tobramycin has been re-prescribed, repeat level on day 2 pre-dose (to ensure dose reduction has been successful)

Repeat of levels thereafter: Weekly
During a 2 week course, more frequent repeat levels should be considered in those with acute pyrexial

illness, vomiting, diarrhoea and any other reason for dehydration or renal impairment (e.g. on concomitant nephrotoxic medication)

Ensure patient's nebuliser is changed to colomycin whilst in hospital if usually takes nebulised tobramycin (Bramitob) at home

5.6 Other antibiotics and nebulisers

Nebulised

1. Colistimethate sodium (Colomycin) – Is given to
- All CF children who are **colonised** with *Pseudomonas*
- All CF children **whilst in hospital regardless of reason for admission.**

2. TOBI® or BRAMITOB ® (tobramycin as a preservative-free preparation made for nebulisation)

This is given on alternate months, sometimes alternating with Colomycin. It is given in patients colonised with *Pseudomonas*, not doing well on maximal treatment, requiring frequent courses of IV antibiotics. Currently this is commenced at BCH.

NB nebulised tobramycin is not given whilst the patient is receiving IV Tobramycin

3. Amikacin
Administration –
For 250mg dose: add 2ml 0.9% saline to 1ml of 250mg/ml injection
For 500mg dose: add 1ml 0.9% to 2ml of 250mg/ml injection

Nebulisers

Drug	DNase	Hypertonic saline	Colomycin (Colistin)	Promixin (Colistin)
Mode of action	Synthetic enzyme which reduces sputum viscosity and aids expectoration	Osmotically draws water into the airways to hydrate mucus and aid clearance	Nebulised antibiotic for treatment of pseudomonas aeruginosa (PsA)	Nebulised antibiotic for treatment of pseudomonas aeruginosa (PsA)
Indications	Considered in all patients > aged 6 FEV1< 85% Persistent wheeze Symptomatic but no sputum Can be considered in pre-school children with concern over respiratory status	Long term mucus hydrator. Cheaper alternative to DNase Short term use in exacerbation to aid removal of thick secretions	First isolation of PsA – minimum 3 month course, twice daily. Colonisation of PsA, twice daily. Prophylactic, once or twice daily. Given for any hospital admission, twice daily	For use only with i-neb. Can download data to check compliance Can only be used with a mouthpiece
Dose	2.5mg once daily	3%, 6% or 7% (most commonly 7%), once or twice daily	1 million unit for children under 2 2 million units (MU) over 2 years, once or twice daily	1 million (MU) equivalent to 2 MU via conventional nebuliser, once or twice daily

Amount	2.5ml	4mls	1 MU: Mix 1 vial with 2-4mls 0.9% NaCl 2 MU: Either 1x 2MU vial with 2-4 mls 0.9% NaCl or mix 2 1MU vials with 2mls 0.9% NaCl in each	1 MU: ½ MU (mix 1 MU with 2mls saline, draw out 1ml) 2MU: mix 1 vial with 1 ml saline
Timing	At least an hour before physiotherapy but not within 1.5-2 hours of nebulised colomycin **Store in fridge**	Before physiotherapy or can be combined with an airway clearance device e.g. aerobika	After physiotherapy, not within 1.5-2 hours of DNase	After physiotherapy, not within 1.5-2 hours of DNase
Pari turbo boy / e-flow	Yes	Via e-flow or turbo boy, leaves 1ml in the chamber	Yes	No
i-neb	Use GREEN latched chamber (1ml fill volume) Fast nebulisation: 1 min	Use LILAC chamber (2 ml fill volume) Need to nebulise 2mls twice	N/A	Use GREY chamber (1ml fill volume) Fast nebulisation, 90s
Need for filtering	No	No	Yes	No. Breath actuated, only emits aerosol on inspiration

When admitted, patient should bring their own nebulisers and compressors, but if they have not got one or have not brought their own, to avoid cross infection their nebulised treatment should be administered via a standard Acorn nebuliser and driven by wall oxygen at > 8 l/min. For nebulized antibiotics, a filtered nebulizer set can be used (e.g. Pari Filter Set) or elephant tubing out of the window.

5.7 Bronchodilators

SALBUTAMOL 100mcg, (2-4puffs) if indicated, should be given before chest physiotherapy in hospital.. Salbutamol should be given by MDI and spacer. If there is an oxygen requirement salbutamol nebuliser should be given as per BNFc doage.

5.8 Inhaled corticosteroids

Before starting inhaled steroids, lung function with reversibility should be considered.
Children taking inhaled Flixotide or Seretide should continue with them at their usual (bd) dose. *The in-patient stay is a good time to check inhaler technique.*

5.9 Oral corticosteroids

A 5-7 day course of PREDNISOLONE 1-2 mg/kg/day (*soluble or non-enteric coated*) is sometimes given. This is usually reserved for the 2nd week if no chest improvement occurs after a week of IV antibiotics. Children may already be on alternate day PREDNISOLONE at a lower dose. The regular dose needs to be reviewed at discharge. Longer courses may be used to treat allergic bronchopulmonary aspergillosis (ABPA).

5.10 Pancreatic enzyme supplements

It is estimated that 90% of CF children have pancreatic insufficiency. The most common way to diagnose this is a faecal elastase level.

Normal	>200mcg/g stool (usually >500)
Mild/moderate pancreatic insufficiency	100-200mcg/g stool
Severe pancreatic insufficiency	<100mcg/g stool
CF Pancreatic insufficiency	<15mcg/g stool

Requirement of pancreatic enzyme replacement therapy (PERT) varies widely and should be assessed on an individual basis following dietary and symptom analysis. Steatorrhoea is usually characterised by oily, floating, grey, yellow or orange stools which can be difficult to flush. This is an indicator that PERT is not optimal. Performing a test for faecal fat globules may be useful if symptoms are present or optimal growth is not being achieved.

Creon contains three different enzymes to aid with food digestion: fat, protein and carbohydrate. The enzyme comes in various strengths: Micro (enteric-coated microspheres) 5000 and capsules 10,000 and 25,000. Creon should be taken whole and generally taken at the start of a meal. The enzymes are most effective 20-30 minutes after they have been swallowed. Between 2-5 years children should be encouraged to move towards the capsules and weaned off Creon Micro.

Creon Micro should be given in a small amount of fruit puree or in some of the mother's breast milk from a spoon. As the enzymes are denatured when exposed to heat they should not be mixed with formula or hot food.

Taking excess amount of Creon could increase the risk of developing colonic strictures especially in the younger patients. **Prescribing excess of 10,000 units of lipase per kg of body weight should be done with caution.**

However some children will require high doses to control their symptoms of Steatorrhoea, especially during periods of accelerated growth. If excessively high doses appear necessary, enzyme efficacy can be improved by using a proton pump inhibitor or H_2 antagonist preferably given 1 hour before meals (use BNFc for doses) to reduce gastric output.

Typical doses of creon micro used in <2years

Age (years)	Scoop per feed
<6 months	½ to 1 scoop per feed
>6 months	1-2 scoops per feed +1 scoop with solids

Typical dosages of Creon 10 000 used at different ages:

Age (years)	Capsules per meal	Daily Creon Capsules
3-4	2-4	8-15
5-6	3-5	15-20
7-8	4-6	18-24
9-10	6-8	26-30
12+	8-10	36-40

Approximately half the dose is needed with snacks, depending on fat content.

5.11 Vitamins

Fat-soluble vitamins (A, D & E) are checked at annual review and supplementation prescribed appropriately.

Standard doses:

<1year of age

o 1st line : 0.6ml Abidec (=Vitamin A 1333 units, Vitamin D 400 units) PLUS Vitamin E (alpha tocopheryl acetate) 25 mg (0.25 ml) OD

o 2nd line : if unavailable or not tolerated Paravit-CF 0.1ml OD

o In exceptional circumstances: Dalivit 0.3ml OD (Vitamin A 2500units, Vitamin D 200 units) can be used temporarily and revert to Abidec/Paravit-CF when possible

>1year age

o 1st line: 1.2ml Abidec (= Vitamin A 2666 units, Vitamin D 800units) PLUS Vitamin E (alpha tocopheryl acetate) 25 mg (0.25 ml) OD

o 2nd line: if unavailable or not tolerated Paravit-CF 0.25ml OD

o In exceptional circumstances: Dalivit 0.6ml OD (Vitamin A 5000units, Vitamin D 400 units) can be used temporarily, revert to Abidec/Paravit-CF when possible

When able to swallow tablets (approx 2-5years of age):

- 1st line: 2 x vitamin A and D capsules (=Vitamin A 8000units and Vitamin D 800units) PLUS transition to nearest Vitamin E (alpha tocopheryl acetate) capsule preparation (usually 75units (50mg) gel cap OD
- 2nd line: if unavailable or suboptimal levels or requiring >3 tablets of vitamin A and D / additional vitamin D switch to Paravit-CF capsule
- 1-8years 1 capsule OD
- >8years 2 capsules OD

Separate additional Vitamin D This may need to be given in patients on reduced vitamin A and D supplements if the vitamin D level is low and/or PTH is high.

Preparation	Quantity of Vitamin A (units) per dose	Quantity of Vitamin D(units)per dose	Quantity of Vit E per dose	Quantity of Vit K per dose
Vitamin A + D caps Per capsule	4000	400	0	

BPC Vitamins per capsule	2500	300	0	
Abidec® 0.6ml	1333	400	0	
Dalivit® 0.6ml	5000	400	0	
Vitamin E Suspension 100mg/ml	0	0	100mg	
Vitamin E Gelcap® 75 units	0	0	75 units or 50mg	
Vitamin E Gelcap® 200 units	0	0	200 units or 134mg	
Vitamin E Gelcap® 400 units	0	0	400 units or 256mg	
Calcichew D3 Forte® Per chewable tablet	0	400 units plus 500mg Calcium		
Cholecaliferol 3000 units/ ml	3000units (most common)	Variable depending on vitamin D levels		
Vitamin A 5000 units/drop	5000 units			
Paravit® CF Liquid (0.1ml OD)	1600 units	600 units	60 units	2mg
Paravit® CF Liquid (0.25ml OD)	4000 units	1500 units	150 units	5mg
Paravit® CF 1 capsule OD	4000 units	1500 units	150 units	5mg
Paravit® CF 2 capsules OD	8000 units	3000 units	300 units	10mg

At annual review the following should be measured on all patients:
Vitamin A, D, E
If abnormal results are seen, the following action should be taken.

- Check compliance and dose (better absorption if taken with food and in tablet form)
- Check no other vitamin supplements are taken and consider vitamins in supplements
- Check vitamin storage at home

If you are satisfied with the response to the above, take the following action:

Vitamin A	**Vitamin D**	**Action**
Low (10% below ref. range)	Low (<50nmol/l)	**Increase** combined Vitamin A and D supplement by 50-100% and recheck levels in 3-6 months
Low (10% below ref. range)	Normal (≥50nmol/l)	**Increase** combined Vitamin A and D supplement by 50-100% and recheck levels in 3-6 months
Normal	Low (<50nmol/l)	**Increase** combined Vitamin A and D supplement by 50-100% and recheck levels in 3-6 months
High (10% above ref. range)	Low (<50nmol/l)	**Reduce** combined vitamin A and D supplement by 50-100%. **Give additional**

		Vitamin D supplement and recheck levels in 3-6 months
High (10% above ref. range)	Normal (≥50nmol/l)	**Reduce** combined vitamin A and D supplement by 50% and recheck levels in 3-6 months

Vitamin E	**Action**
Low (<11.5 micromol/l)	**Increase** supplement by 100% and recheck level in 3-6 months
High (> 30 micromol/l)	**Reduce** supplement by 50% and recheck in 3-6 months

5.12 Salt

Oral SODIUM CHLORIDE supplementation is normally given during the summer 18-20 ºC. In children aged less than 1 year it is given all through the year. It can also be considered all year round if joint pains or muscle cramps are a problem. The dosage is approximately halved for those patients taking CFTR modulators.

The dosage is according to age:

For children who can swallow tablets/capsules, SLOW SODIUM tablets (600 mgs =10 mmol Na)

2 to 5 years: Slow Sodium tablets (600 mg) one tablet once (to twice) a day
If taking CFTR modulator one tablet once daily

5 to 10 years: Slow Sodium Tablets (600 mg) one tablet twice daily
If taking CFTR modulator one tablet once daily

10 years & over: Slow Sodium Tablets (600 mg) one tablet three times a day
If taking CFTR modulator one tablet twice daily

For babies and young children who are unable to swallow tablets, SALT SOLUTION (1mmol/ml, 1mmol=58.5mg Na):

Below 2 years: 2 mmol/kg/day in 2 or more divided doses
(Maximum dose 20mmol per day)

2 to 5 years: 0.5 to 1 mmol/kg/day in 2 or more divided doses
(Maximum dose 10- 20mmol per day)

See appendix 7 for CF salt letter to be sent to GPs

5.13 Ursodeoxycholic acid

CF patients with liver disease are usually on URSODEOXYCHOLIC ACID. Use BNFc for doses.

6 CFTR Modulators

Modulators comprise two groups of small molecule oral drugs:

- **Potentiators** which require the CFTR protein to be in its correct location at the cell surface, and then increase the time the channel spends open. These were originally used in patients with gating (Class 3) mutations which lead to channels which are largely closed; they are also used to increase the activity of CFTR which has been 'corrected' with other molecule(s). This is ivacaftor.
- **Correctors** improve trafficking of misfolded Phe508del CFTR (and some other variants) through the cell to the surface. Those which were tested on their own in clinical trials were inadequately effective unless combined with a potentiator. Three correctors are now licensed: lumacaftor, tezacaftor and elexacaftor which are used in combinations with ivacaftor.

The full lists of eligible genotypes as approved by NHSE are provided on Future NHS website – https://future.nhs.uk

6.1 Potentiator: Ivacaftor (Kalydeco)

Only one potentiator drug is currently licensed. Ivacaftor is approved from the age of 4 months (for those with one or more gating mutations (G551D, G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P, G1349D); NHS England have widened the list for which funding is available based on FDA approval of a range of lab-sensitive mutations. Currently, adults and post pubertal children (essentially 14 years and above) with R117H are eligible for treatment. However, this only applies to those with CF disease and evidence of abnormal CFTR Function.

6.2 Correctors / potentiator combinations

The commonest CF gene variant, Phe508del, results in CFTR protein which does not reach the cell surface; one or more correctors are used to assist trafficking of the protein to the cell surface and ivacaftor then further enhances CFTR function. Three combination treatments are currently available:

Lumacaftor / ivacaftor (Orkambi)

Clinical trial improvements were more modest than those seen with ivacaftor (2-3% FEV1) but impacts on rate of pulmonary exacerbation were more robust. It is currently available for children 1 year and older who are homozygous Phe508del. In practice it is used for younger children, as those aged 2 and above can receive Kaftrio (below) which is more effective. In older patients, chest tightness was a relatively common early side effect; this seems less of an issue in younger children with earlier stage disease.

Tezacaftor/ ivacaftor (Symkevi)

The second dual combination demonstrated similar efficacy to Orkambi but improved tolerability fewer drug-drug interactions. It is licensed for people from 6 yrs of age who are homozygous Phe508del and have one of the following mutations:

P67L, R117C, L206W, R352Q, A455E, D579G,711+3A→G, S945L, S977F, R1070W, D1152H,2789+5G→A, 3272-26A→G, and3849+10kbC→T. Or children with selected 'rare mutations' as approved by NHSE CFTR modulator commissioning policy.

Elexacaftor/ tezacaftor/ ivacaftor (ETI, Kaftrio)

This is now licenced from the age of 2 years (Nov 23) Eligible population (based on EMA license plus a group granted access by NHS England in line with FDA approval:

- Any patient with at least one Phe508del
- Patients without Phe508del, possessing at least one of a range of other mutations

All children reaching this age and on Orkambi will be switched to Kaftrio. Children receiving ivacaftor will likely gain further benefit from Kaftrio if they fall into the groups above. Families should be counselled to this effect and switched over unless a good reason exists not to.

Prior to starting Receive Orkambi® OR Symkevi® OR Kalydeco® OR Kaftrio® a contract will be signed by the patient and family and BCH CF team to ensure that patients are compliant to all existing treatment.

Modulator therapies are prescribed and home delivery arranged by the BCH CF team

Before starting treatment, patients will:

- Have a weight, lung function, liver function tests and confirmation of correct genetic mutations.
- Have an eye test performed.
- Be seen by the prescribing doctor at the start of treatment.
- Be given supporting written information regarding the new medication.
-

Once treatment is established, patients will:

- Receive Orkambi® OR Symkevi® OR Kalydeco® OR Kaftrio® via home delivery.
- Weight, lung function and quality of life questionnaire must be carried out one month after starting treatment.
- Liver function blood tests, weight, lung function and must be monitored at 2-3 months after starting treatment.

Patients will then have blood tests for liver function 3 monthly for the first year and then yearly.

Patients will be reviewed at Birmingham Children's Hospital at least 6 monthly following commencement of treatment.

- **Caution is required when prescribing potential interacting drugs including itraconazole, rifampicin and clarithromycin as well as St John's Wort, grapefruit and Seville oranges.**

- **When initiating modulators in patients taking strong CYP3A inhibitors e.g. itraconazole or clarithromycin, the dose should be reduced please see BNFc.**

- Caution in liver impairment and severe renal impairment see manufactures summary of product characteristics for recommended dose adjustments and speak to pharmacy for further advice.

Dosage for CFTR modulators

Doses need to be increased once weight thresholds are reached
Twice daily tablets or granules have to be taken with fat containing food.

Dosing recommendations for Ivacaftor for patients aged 4 months and older.		
Age	**Formulation**	**Ivacaftor ORAL dose**
4-5 m >/= 5kg	≥5kg: ivacaftor 25 mg one **sachet** morning and evening	One **sachet** every 12 hours
6m-17y	5kg - <7kg: ivacaftor 25mg one **sachet** morning and evening	One **sachet** every 12 hours
	≥7kg - <14kg: 50mg ivacaftor one **sachet** morning and evening	One **sachet** every 12 hours

	≥14kg - <25kg:75mg ivacaftor one **sachet or tablet** morning and evening	One **sachet** or one **tablet** every 12 hours
	≥25kg: 150mg tablet ivacaftor one **tablet** morning and evening	One **tablet** every 12 hours

Dosing recommendations for Orkambi for patients aged 1 year and older.		
Age	**Formulation**	**Orkambi ORAL dose**
1-5 years	≥7kg - <9kg: Lumacaftor 75mg /ivacaftor 94 mg one **sachet** morning and evening	One **sachet** every 12 hours
	≥9 kg- <14kg: lumacaftor 100 mg/ ivacaftor 125mg one **sachet** morning and evening	One **sachet** every 12 hours
	≥14kg lumacaftor 150 mg/ ivacaftor 188mg one **sachet** morning and evening	One **sachet** every 12 hours
6 to 11 years	Two lumacaftor 100 mg/ ivacaftor 125mg **tablets**	Two **tablets** every 12 hours
12 years and older	Two lumacaftor 200 mg/ ivacaftor 125mg **tablets**	Two **tablets** every 12 hours

Dosing recommendations for Kaftrio (ivacaftor/tezacaftor/elexacaftor)for patients aged 1 year and older.		
Age	**Formulation**	**Kaftrio ORAL dose**
2-6 years	<14 kg Kaftrio (60/40/80mg) one **sachet** in the morning and Ivacaftor 59.5mg one **sachet** in the evening	One **sachet** every 12 hours
	>14kg Kaftrio 75/50/100mg one sachet in the moning And Ivacaftor 75mg one **sachet** in the evening	One **sachet** every 12 hours
6 years+	< 30kg 2 kaftrio **tablets** (37.5/25/50mg) in the morning 1 ivacaftor **tablet** (75mg) in the evening	Two **tablets** in the morning and one in the evening
	≥30kg: 2 Kaftrio (75/50/100mg) **tablets** in the morning And 1 ivacaftor 150mg **tablet** in the evening	Two **tablets** in the morning and one in the evening

Dosing recommendations for Symkevi for patients aged 6 years and older.		
Age	**Formulation**	**Symkevi ORAL dose**
>6 y	<30kg 1 Symkevi **tablet** (tezacaftor 50mg/ ivacaftor 75mg) in morning And 1 ivacaftor 75mg **tablet** in the evening	One **tablet** every 12 hours
	>30kg Symkev (tezacaftor 100mg/ivacaftor 150mg) 1 **tablet** in the morning And 1 Ivacaftor 150mg **tablet** in the evening	One **tablet** every 12 hours

6.5 Information on taking CFTR modulators

CFTR modulators need to be taken 12 hours apart and with food or drinks that contain fat. Most people will find that taking the medicine with breakfast and a bedtime snack is the easiest way to do this.

Examples of fat-containing foods:
Fat-containing breakfast ideas:

- Cereal with full fat milk
- Slice of buttered toast
- Slice of toast or ½ bagel with peanut butter, Nutella, full fat soft cheese or avocado
- A slice of cheese on toast
- Buttered crumpet
- A Croissant
- A Boiled egg

Fat-containing snack ideas:

- Glass of full fat milk
- Pot of full fat yogurt
- Handful of nuts (for children over 5yrs)
- Cracker with cheese
- Cereal bar
- Bag of crisps
- Chocolate bar
- Nutritional supplement (if they are prescribed)

Missed Doses

- If a dose is missed; if less than 6 hours have passed since the missed dose, the scheduled dose of the Kalydeco/Orkambi/symkevi/kaftrio should be taken with fat-containing food. If more than 6 hours

have passed, the patient should be instructed to wait until the next scheduled dose. A double dose should not be taken to make up for the forgotten dose.

***Drug interactions*:** There are some significant interactions, most importantly:

Itraconazole, voriconazole: lead to inhibition of the breakdown pathways of precision medications and accumulation of the drug. If co-administration is necessary, the dose of the precision medication should be reduced.

Clarithromycin: also leads to accumulation of the drug. There is no interaction with azithromycin so this should be used instead.

High dose corticosteroids: may significantly decrease serum levels of the precision medications and reduce efficacy.

Rifampicin: will significantly reduce ivacaftor levels; co-administration not recommended.

St John's Wort: as for Rifampicin.

Grapefruit (or juice) and **Seville oranges** (realistically, this is only marmalade; edible oranges are all fine): should be avoided as they reduce serum levels of ivacaftor.

Hormonal contraceptives, including oral, injectable, transdermal, and implantable, should not be relied upon as an effective method of contraception when co-administered with Orkambi.

6.6 Monitoring for CFTR modulators

- Liver function tests need performing every 3 months for the first year but can then be done with annual bloods
- Ongoing ophthalmology / optician screening (at 12m)
- Sweat tests are repeated annually (done at BCH)

7 Flu vaccination

All children with CF should have an annual flu vaccine. This is usually prescribed by the patient's own GP and done in the GP setting or is done as part of the routine immunisation programme in school for primary school age children.

Age 6 months to 2 years the IM vaccination (inactivated quadrivalent influenza vaccine) should be offered. Those who have not received influenza vaccine previously should be offered a second dose of vaccine, at least four weeks later.
Children aged two to 18 years of age should be offered the nasal flu vaccination (Live attenuated Intranasal Vaccination or LAIV). For primary school children this can be given at school as part of the usual immunisation programme.

Those children who have never received influenza vaccine before and are aged between two and less than nine years should be offered a second dose at least four weeks later.

See BNFc for doses.

Contraindications to the nasal flu vaccination (LAIV):
High dose systemic steroids for over a month: Individuals treated with systemic steroids for more than a month at a dose equivalent to prednisolone at 20mg or more per day or a dose of 1mg or more per kg per

day should not be given the nasal flu vaccination. Inhaled steroids are not a contraindication.

Increased wheeze or required additional bronchodilator treatment in the previous 72 hours. These children should be offered a suitable inactivated IM influenza vaccine to avoid a delay in protection

Cautions / contraindications to all flu vaccinations

Children with an egg allergy – including those with previous anaphylaxis to egg – **can be safely vaccinated with LAIV in any setting** including primary care and schools. (The ovalbumin content of LAIV has been reduced since 2016 to ≤0.024 micrograms per 0.2ml dose, where a very low ovalbumin content is <0.12 micrograms/ml - equivalent to <0.06 micrograms for a 0.5 ml dose.) The only exception is for children who have required admission to intensive care for a previous severe anaphylaxis to egg.

Children who have required **admission to intensive care for a previous severe anaphylaxis to egg** should be given nasal LAIV in the hospital clinic setting or another very low ovalbumin content vaccine. The ovalbumin content of influenza vaccines will be published each year prior to the influenza season.

None of the influenza vaccines should be given to those who have had: **a confirmed anaphylactic reaction to a previous dose of the vaccine.**

Please see the Green Book for immunisation for the most up to date advice on flu vaccination. https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book

8 Totally Implantable Venous Access Devices (Tivads/"Vascuports"/"Port-A-Caths/Cvad")

Many children have Vascuports if they require bloods or IV antibiotics frequently.

8.1 Inserting Vascuport needle
Please refer to the Trust Guideline

In order to access a Vascuport you will have received specific training and must be deemed competent.

Prior to accessing the port, it should be palpated to ensure correct positioning (the port can be just below the clavicle or in the anterior axillary line). Ensure the correct size needle is available. Some children require longer needles if the Vascuport is particularly deep. The size needed should be documented in medical notes otherwise ask parents/carers.

Topical anaesthetic such as Ametop, EMLA or cold spray should be offered and allowed enough time to work prior to insertion.

An aseptic non-touch technique (ANTT) must be used when inserting a port needle into
the vascuport. The skin above and surrounding the port must be cleaned for 30 seconds using 2%CHG in 70%IPA (Chloraprep) and allowed to dry for a further 30 seconds. Once this area is cleaned it must not be touched prior to needle insertion.
The 22G needle should then be inserted at a 90 degree angle and once inserted the positioning and patency should be checked by drawing 3-4mls of blood back, if patent flush with 0.9% saline.

The needle should then be secured with an clear tegaderm dressing allowing observation of the site, the site should be observed and documented after every intravenous drug administered or if receiving continuous therapy this should be documented at least every 12 hours.

If the dressing becomes soiled or loose this should be changed. To do this, remove the dressing if still insitu, clean skin around the needle insitu for 30 seconds using 2%CHG in 70%IPA (Chloraprep) and allow to dry for 30 seconds. Secure inserted needle with another clear tegaderm dressing.

The needle should be changed after 2 weeks if the patient is still receiving continuous treatment. If the patient is immunosuppressed then the needle should be changed weekly during continuous treatment (BCH, 2014).

8.2 Accessing port line (when needle in place)

Please refer to the Trust Guideline WAHT-TP-049 Implanted Central Venous Access Device (Alternatively called a port) in Children

An aseptic non-touch technique is used anytime the line is accessed. Prior to accessing the line, the device must be cleaned with a sterile 2% CHG in 70%IPA medical device wipe for 30 seconds and allowed to dry for a further 30 seconds.

The Orchard Nurses and some of the ward nurses are able to access the lines. **Please don't access a Vascuport unless you have been shown how to do it and deemed competent.**

8.3 Outpatient routine flushing – using ANTT

- Done by the Orchard Nurses or CF Nurse Specialists every 4 weeks (often coinciding with clinic appointments where possible).

- (See inserting vascuport needle) Use a 22G non-coring Vascuport needle with attached catheter, insert appropriate length vascuport needle and draw back 3-4mls of blood. Once line patency has been established flush port with 0.9% saline and then instil correct dose of heparinised saline 100u/ml clamping whilst last 0.5mls is instilled. Vascuport needle will then be removed.

8.4 Heparin doses for Vascuport

(unless otherwise advised by the manufacturer (EPIC 2014, BCH 2014)).

Child aged 1year-8years: 2mls heparinised saline 100units/ml
(or use 10 units/ml if higher strength not available)

Child aged 8years and above: 4mls heparinised saline 100units/ml
(or use 10 units/ml if higher strength not available)

8.5 Administration of IV antibiotics via Vascuport – using ANTT

Given via 22G non-coring Vascuport needle (as above).

- Clean using ANTT technique and ensure good blood return (as above).

- Flush vascuport with 0.9% saline.

- Administer intravenous antibiotics as prescribed. If administration is via a bolus use a pulsating action to prevent line blocking.

- If administration is via an infusion follow hospital policy.

- Flush after use with 0.9% saline.

- If the vascuport is being accessed within 12 hours then Heparin is not required.

- If the vascuport is being accessed more than 12 hours later instil 2-4ml heparinised saline 100 unit/ml (as dosing above).

- Close off with a needleless bung.

Needle removal

Please see guideline WAHT-TP-049 Implanted Central Venous Access Device (Alternatively called a port) in Children (in the paediatric haematology / oncology guidelines)

9 Long Lines

9.1 "Short" long lines (e.g. Leaderflex 22G Vygon) –Using ANTT

EQUIPMENT
Single dressing pack (+ 2 extra sterile towels) Sterile gloves
5ml syringe x 2/green needle
Long line
Clear dressing
(2 extra pack gauze swab)
Chloroprep (2% CHG and 70% IPA solution)
1 needleless bung
3 wide Steristrips
Flush solution: 5 ml Normal Saline and 4ml Canusal (100u/ml)

'Short' long lines are usually preferable. They are inserted by a Seldinger technique via a blue cannula. They should be inserted using ANTT precautions. A 96hour filter is generally used to prolong life of the long line – the use of a filter will be advised by the CF team.

Once inserted, they may be used for blood sampling in the first 24 hours (but not for Tobramycin levels- these should be taken by preferably fingerprick or by other venous access, otherwise a spuriously high result may be obtained).

9.2 Sedation or Entonox for long line insertion (or any venous access)

This may be necessary in some patients, particularly if they have had problems in the past and if they are likely to require frequent courses of IV antibiotics. However, not all patients having venous access require sedation.

9.3 Thrombophlebitis

There is some anecdotal evidence for the use of hydrocortisone in long lines complicated by thrombophlebitis. It is not suitable for blocked lines. It appears to be safe and can be repeated as necessary. The steroid dose is minimal so there should not be any steroid adverse effects. If it is going to work it will usually do so after 24 hours.[1]

- Give IV antibiotics in the usual way.
- Use 3 mg hydrocortisone made up to 3 mls (with 0.9% normal saline) into the long line.
- Leave in line until next dose of IV antibiotic.
- Aspirate and flush line in the usual way prior to IV antibiotic.
- Concurrently use 0.5% or 1% hydrocortisone cream topically on arm (over erythematous area).
- Consider using urokinase if long line or TIVAD/PORT is blocked

1 Royal Brompton & Harefield NHS foundation trust. Clinical Guidelines: Care of children with Cystic Fibrosis. 2017. Available at https://www.rbht.nhs.uk/childrencf

10 Annual Bloods

All children attending the CF clinics should have annual blood screening. If this is due around the time of an admission it can usefully be done:

~ during insertion of a long line or Vascuport needle

~ when taking TOBRAMYCIN levels

10-12ml of blood should be sufficient for the following tests:

There are CF blood panel tabs on the paediatric ICE request page

Test	Bottle (colour)	Volume
FBC	EDTA (pink)	0.5ml
Clotting screen	Blue /clear	1.8ml
U & Es Cr Cl Ca Mg PO_4	Gold	2ml
Alb ALP Bili AST/ ALT GGT		
Glucose	Grey	0.5ml
Vit A, D and E	Gold	1 - 2 ml

Samples for vitamins need to be protected immediately from light. Sample tube should be put immediately into a brown envelope.

Biochemistry IgG, IgA, IgM, Gold 2ml -every 3 years

Pseudomonas antibodies – only to be sent on patients who are on nebulised antipseudomonal antibiotics to guide continuation of treatment.

Other bloods which may need to be done on an individual patient basis include:
HbA_1c (in diabetics), specific IgE to aspergillus (if possible ABPA), varicella antibodies,

11 Chest X-Rays

Most children have chest x-rays every 12 months. Check when the latest was taken and whether another would be useful. A PA film only (from August 2020) is required to do a Chrispin Norman score (once a year). These can be done locally, but will need to be sent via PACS and a reporting request form sent to BCH.

See Appendix 8 for CN scoring request form

12 Screening for Hyperglycaemia

See the Screening and Diagnosis of Cystic Fibrosis Related Diabetes (CFRD) Guideline jointly published by the West Midlands Paediatric CF Network and the Children's and Young People's West Midlands Diabetes Network

CF related diabetes (CFRD) is a recognised complication of CF. Ketoacidosis is rare. Children should be screened for glucose intolerance at every admission, particularly if taking regular oral corticosteroids. Initially this should be done by doing a capillary blood sugar 1 hour after every meal for the first 24 hours of the admission (3 measurements) and at 2am if on overnight feeds.

A raised random glucose level indicates impaired glucose tolerance. Mildly or intermittently elevated blood glucose levels need watching and may require further continuous glucose monitoring at home, an OGTT (oral glucose tolerance test) or the reduction of Prednisolone. If Prednisolone is started or the dose increased during admission, the BM profile may need to be restarted.

An extended OGTT can be done at Children's clinic WRH as a day case with bloods taken at baseline (fasting glucose), 30, 60, 90 and 120 minutes post glucose solution. Please discuss with children's clinic.

Patients with frank diabetes (markedly raised levels, polyuria, weight loss, etc.) should be referred to the Diabetic Team and treated with insulin.

13. Chest Physiotherapy

13.1 Airway Clearance Techniques

A physiotherapist is available in clinic to assess all patients and discuss and review their physiotherapy management. The airway clearance techniques (ACT) used vary within age groups and are always assessed on an individual basis:

Babies and infants– Techniques taught may include modified gravity assisted positioning (no head down position) and percussion in 5 positions (alternate sides, prone, supine and upright); as well as infant positive expiratory pressure (PEP). Gym ball bouncing with the baby/child positioned safely on the parents lap can be used to encourage change in lung volumes.

2-3 years and upwards – Begin with blowing games and Bubble PEP. Encourage deep inspiration and a long breath out as able.

4-5 years and upwards – Encourage more independent treatments using a full variety of airway clearance devices and techniques as appropriate (with family support /supervision).

The frequency and duration of ACT will alter depending on infective exacerbations, severity of disease and individual circumstances. In the majority of cases twice a day for 15-20 minutes is the minimum recommended.

Airway clearance techniques taught include:

- **Active Cycle of Breathing Techniques** (ACBT) – Combination of thoracic expansion exercises, breathing control, and forced expiration techniques.

- **Blowing games -** ideas include blow football, blow painting, bubbles and whistles. Bubble PEP requires blowing into a volume of water (10-20cms) via a 40cm tube to create bubbles. The inner diameter of the tube should be 8mm (use suction tubing). The water provides resistance to expiration and therefore creates positive expiratory pressure and oscillation in the airways to mobilise secretions.

- **Positive Expiratory Pressure** (PEP) – Provides resistance to expiration through a mouthpiece or facemask, which temporarily increases functional residual capacity, encouraging collateral ventilation and alveolar interdependence, to recruit closed airways and get air behind secretions. This is followed by forced expirations.

- **Low pressure PEP** – PEP applied via a mouthpiece or mask, and is usually undertaken in the sitting position. Breathing through the device should be at tidal volume with slightly active expiration. A manometer can be inserted between the expiratory valve and the resistor to measure mid-expiratory pressure which should be 10-20 cm H2O

- **Infant PEP** – PEP adapted for infants via a mask over the child's nose and mouth. Performed in the caregiver's arms or seated on their lap, bouncing on a gym ball. A pressure of 10-20 cm H2O should be achieved.

- **High Pressure PEP** – 8-10 regular PEP breaths followed by forced expiration into the PEP mask. This creates pressures of 40-100 cmH2O and will therefore not be appropriate for all patients.

- **Oscillating PEP devices (e.g. Acapella, Aerobika, Cornet, Flutter):** Creates positive expiratory pressure and oscillation on exhalation to prevent premature airway closure, mobilise secretions, improve airway patency and reduce sputum viscosity.

- **Autogenic Drainage (AD) –** Uses controlled breathing which aims to attain the highest expiratory airflows to move secretions from peripheral to central airways while avoiding coughing and significant airway closure/or compression. Breathing is usually from low to high lung volume where secretions are expectorated.

- **HFCWO (Vest)** – **High Frequency Chest Wall Oscillations**. Extra thoracic oscillations are generated by forces external to the respiratory system. An inflatable jacket or strap fits around the chest; oscillations are transmitted to the chest wall at approx. 14Hz. This enhances mucociliary transport by creating a cough-like expiratory flow bias that shears mucus from the airway walls. There is no clear evidence between HFCWO and other airway clearance techniques and cost of this device can be prohibitive. However, it should be considered where adherence to other airway clearance techniques is problematic.

13.2 Physiotherapy and inhaled medications

Bronchodilators - pre-physiotherapy if necessary and benefit shown. No need to do this routinely 10-15 mins before physiotherapy, effect can be quite fast so quicker for child if use it at time of physiotherapy session.

Hypertonic Saline - Immediately pre-physiotherapy but post bronchodilator. Can also be given during airway clearance if combined with PEP or oscillating PEP. This can save the patient time, but may reduce the total lung deposition

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DNase – Timing is decided on an individual basis. In most cases it is given at least 1 hour pre-physiotherapy. N.B some children take it 1-2 hours pre-physiotherapy and a few even longer, occasionally we recommend it is taken before bed but this is a *consultant decision* and coughing overnight should be carefully monitored.

Steroid Inhalers – Usually taken post physiotherapy treatment. NB rinse mouth after taking a steroid or combination inhaler.

Inhaled antibiotics - Post-physiotherapy. Either dry powder inhalers or nebuliser

Inhaled medication should be co-ordinated with physiotherapy

13.3 Exercise

The importance of exercise throughout the patient's life is highlighted in clinic, on the ward and at home visits. Evidence links exercise capacity to improved survival, and therefore exercise forms a key part of treatment and should be carried out alongside ACT. Current thinking is that exercise should happen between 3 to 5 times per week, lasting for a minimum of 30 minutes per session. Exercise needs to be done consistently, easily fit into the patient's lifestyle, be social, give positive feedback and have realistic goals. The aim is to exercise to a target heart rate of 65% of maximal heart rate for the child's age.

13.4 Posture - Assessment, education and treatment is provided at each intervention where required.

13.5 Urinary incontinence

Stress incontinence can occur even in young children during activities such as coughing, laughing and exercise. This can be assessed by the CF physiotherapist and may be referred on for more specialist advice by the Pelvic Health team.

14 Induced sputum

Sputum induction may be requested for those who have declining lung function and are non-productive of sputum, with no significant bacterial growth, before resorting to a bronchoscopy and Bronchial-alveolar lavage (BAL)

An appointment for sputum induction takes approximately 1 hour and can be performed in Children's Clinic by the Physiotherapists and/or Specialist Nurses.

It involves the child inhaling 7% (6% if 7% not available) hypertonic saline for 15 minutes via a nebuliser (ultrasonic nebuliser is recommended). Where possible, a sputum specimen will be collected and sent for microbiology. If the child is unable to expectorate, a cough swab and sample via oral catheter suction and sputum trap is performed. A bronchodilator can be administered prior to the test if required.

Spirometry is performed before and after the nebuliser to ensure no adverse effects i.e. bronchoconstriction. The child will be asked to huff and cough and carry out airway clearance techniques to expectorate secretions.

The test can also be performed in younger children who cannot carry out spirometry; in this case, oxygen saturations and auscultation is used to monitor throughout the process.

Induced sputum should be stopped if SaO2 < 90% or if the patient is showing signs of bronchospasm.

Precautions should be considered regarding infection control. PPE should be worn by the clinicians, and if possible the room should remain empty following the procedure for as long as possible.

15. Microbiology and Cross Infection

Whilst in hospital, **patients should have a sputum / cough swab sent off once a week.** The sputum is the "gold" standard but if not available, cough / cough swabs should be sent. Antibiotics may need to be changed according to current sensitivities. In those patients with deteriorating lung function/ increased symptoms, a **sputum** specimen may be required to be sent to rule out infection by non-tuberculous mycobacterium.

The identification of potentially transmissible pathogens in the respiratory secretions should be communicated promptly to all teams caring for the patient in a timely fashion. Successful eradication should also be communicated to all teams. Eradication would be defined as 3 clear samples at least 48 hours apart when off treatment. For NTM this would be from sputum or BAL only. Transient colonisation of B cepacia and NTM have been seen. Patients are considered infection free 1 year after having at least 3 negative samples after the last positive isolate.

15.1 MRSA screen

If isolated in respiratory secretions, a full screen should be done. A full screen includes: Nose, throat, perineum, umbilicus (neonates), wounds and other skin lesions, sites of indwelling intravascular devices (if present), catheter urine (for patients with indwelling urinary catheters only), tracheostomy site (if present) and other sites that were previously positive e.g. cough swab/sputum.

Patients with MRSA in respiratory/surface cultures should be isolated when in a hospital setting. They should be reviewed **at the end of a clinic in a separate room** which is deep-cleaned afterwards unless all cultures from the MRSA screen are negative on 3 consecutive occasions (samples must be collected at least 48 hours after completion of decolonisation treatment, or any other antimicrobial therapy active

against MRSA, has ceased). MRSA screens must be collected at least a week apart.

Eradication should be attempted at **1st isolation** with 2 weeks of an antibiotic or a combination to which it is sensitive. Please see BNFc for dosing, rifampicin or fusidic acid should not be used alone because resistance may develop rapidly. 5 days of topical nasal treatment e.g. mupirocin should be applies to the anterior nares and 4% chlorhexidine gluconate for daily bathing.

15.2 *Burkholderia cepacia*, *MRSA, mycobacterium abscesses* and multi-resistant *Pseudomonas* colonisation

Those with MRSA or multi- drug resistant Pseudomonas should be source isolated in a cubicle using standard source isolation precautions.

Due to the risk of cross-infection, patients with B.cepacia colonisation should be nursed in a cubicle with ensuite bathroom with strict isolation nursing. They should be seen in a separate outpatient clinic.
Any new isolate of B. cepacia should be sent to PHE, Colindale for typing. Please liaise with local microbiologist to request this. Eradication should be attempted with 2 weeks of intravenous antibiotics.

Non-tuberculous mycobacteria (NTM)
Due to the potential risk of cross-infection, patients with NTM infection should be nursed in a cubicle with ensuite bathroom with strict barrier nursing. They should be seen in a separate outpatient clinic.
Any new isolate of NTM should be sent to PHE, UHB (Heartlands) for typing and antibiotic sensitivities. Please liaise with local microbiologist to request this and inform Dr Desai. Microbiology contacts at BCH are Phil Milner/Dr Mitul Patel (Microbiology BCH).
Clinical management should be according to the ECFS/CFF guideline.

15.3 Aspergillus Lung Disease

Aspergillus fumigatus is a fungus that grows at 37°C. and the spores are of a size that they are deposited in the distal airways. The fungus produces a large number of toxic and allergenic exoproducts. There are a large number of manifestations in CF. Children are advised to avoid mucking out stables.

Allergic bronchopulmonary aspergillosis (ABPA) is a serious potential cause of lung damage and is not uncommon in CF (prevalence varies 0.6 - 11%). Early pick-up depends on screening and high clinical suspicion. There are rare reports of an ABPA-like picture being a complication of other strains of *Aspergillus*, and other fungi, such as
Scedosporium apiospermum.

Diagnostic criteria - This can be a very difficult diagnosis to make, because in the context of CF, most of the major and minor criteria can be positive in the absence of ABPA. Atypical
cases may lack some or all of these criteria – maintain a high index of suspicion.

Clinical –

- Increased wheezing/chestiness particularly if failing to respond to antibiotics and inhaled medications.
- Fever and malaise.
- Thick sputum with brown or black bronchial casts.

Investigations –

- *Major Criteria*
- CXR pulmonary infiltrates > 1cm diameter and segmental collapse.

- High serum IgE - especially an abrupt recent 4-fold rise to above 500 iu/ml, which falls with prednisolone therapy.
- High specific aspergillus IgE RAST. The normal value <0.35 iu/ml may rise 10-100x in ABPA.
- Positive aspergillus IgG (ICAP) >90 is positive in CF.
- Eosinophilia (> 0.4 x 109/l).
- Positive skin prick test to aspergillus antigen (3mm > control).
- Reversible bronchoconstriction.
- Central bronchiectasis.
- *Minor Criteria*
- *Aspergillus fumigatus* culture from sputum (NB found in 30% of all CF patients).
- Brown/black plugs in sputum.
- Late skin test reaction.

Treatment -
Oral corticosteroids.
Treatment is with corticosteroids to address allergic inflammation together with antifungal therapy to reduce antigen burden and act as a steroid sparing agent. Oral prednisolone is the preferred corticosteroid, given in the morning after food (not enteric coated as it is not well absorbed in CF), with dosing as below:

- 1mg/kg (maximum 40mg) OD for 1 weeks
- 0.5mg/kg (maximum 20mg) OD for 1 week
- 0.5mg/kg (maximum 20mg) alternate days for 2 weeks
- 0.25 mg/kg (maximum 10 mg) alternate days for 4 weeks and then review
- Then gradual reducing course to stop over 2-6 months guided by clinical response and IgE. Relapse is common within 2-3 years of the first episode.

Pulsed methylprednisolone IV methylprednisolone 10-15 mg/kg ONCE per day for 3 days every month has been used, maximum dose 1g, usually for 3 months. The use of methyprednisolone should be a consultant decision in discussion with the BCH CF team.

Antifungals
Itraconazole is used routinely for treatment of ABPA, in combination with oral or intravenous corticosteroids.

Starting Itraconazole dose is 5mg/kg/day (max 200mg) given once a day for 3-6months. Doses can be increased to 10mg/kg/day (max 400mg/day), usually given in divided doses, if necessary.

Absorption is poor orally, and the oral suspension should be used if patients will take it (as it is absorbed better), otherwise capsules can be used. Omeprazole and ranitidine should be stopped if possible.

Administration**:**
Itraconazole suspension should always be taken on an EMPTY stomach and patients should not eat for 1 hour after administration. Capsules are only used when patient do not tolerate the liquid (often due to poor taste) due to their poor availability. Capsules should be taken WITH or immediately AFTER food and taken with an acidic drink i.e. Coca-Cola or Orange juice to aid absorption.
Monitoring:
Baseline Liver Function Tests (LFTs) should be reviewed prior to initiation of itraconazole (due to association with hepatitis and impaired LFTs). Repeat LFTs after 3 months should be considered in patients at risk of liver impairment.

Itraconazole levels may be assayed if there is a poor treatment response – these are sent to Bristol for analysis.

Beware of drug interactions e.g., with orkambi, symkevi, kaftrio, rifampicin, omeprazole.

16. Haemoptysis in CF

Streaky haemoptysis is common with chronic infection but may indicate deterioration so sputum should be cultured and a course of antibiotics considered. The source is usually from hypertrophied tortuous bronchial arteries supplying areas of chronic airway inflammation.

Also consider whether this could be haematemesis and consider the possibility of pulmonary embolism if the child has a port. The patient may experience a gurgling sensation which is a reliable lateralising symptom indicating the bleeding site. The patient is likely to be very scared - reassurance is essential.

Massive, profuse haemoptysis due to vessel rupture can be life-threatening but is rare. Anything more than half a cupful over 24 hours should be discussed with the respiratory consultant on-call at BCH as should persistent bleeding over several days. Massive haemoptysis has been associated with Staph aureus infection.

Management

- Reassurance – the patient and family are very likely to be scared
- Resuscitation if needed (incredibly rare) - lay patient on the side (gurgling side down), give oxygen.
- Consider other sources haematemesis, bleeding from nose or mouth, pulmonary embolism if the child has a port
- Stop NSAIDs
- Consider stopping hypertonic saline if significant haemoptysis. No evidence that stopping DNase is necessary, but this may be considered if profuse haemoptysis.
- Physiotherapy may have to be adapted - seek advice
- **Investigations:**
    - Hb and platelets, Coagulation, Group and save or cross-match blood,
    - Sputum culture.
    - Consider CXR - can show new infiltrates but may not change management and is of little use locating bleed
- Consider course of antibiotics

- **<u>Profuse haemoptysis:</u>**
- Give blood and correct coagulation defects if necessary (IV vitamin K/ FFP / cryoprecipitate).
- Start intravenous antibiotics; *S aureus* cover must be included.
- Early discussion with BCH

Physiotherapy management in the presence of haemoptysis

(Adapted from CF Trust guidelines on physiotherapy management 2011)	
MILD Streaking or <5mls in 24 hrs. Sputum and blood mixed together	• Reassurance • Normal airway clearance regimen
MODERATE 5mls to <250mls blood in 24 hours Fresh blood 1 white sputum pot = 250mls	• Airway clearance techniques should minimise increases in intrathoracic pressure. • Airways clearance with ACBT or AD initially. • Minimise unproductive coughing. • Positioning – see below. • Avoid moderate and high-intensity exercise. • Continue nebulised DNase. • Consider stopping HTS or mannitol if causes coughing – discuss with senior. • Graded approach to reintroduce ACT if no further bleeding – in discussion with senior.
SEVERE > 250mls blood in 24 hours	• Urgent medical review. • Position patient with bleeding lung down. • Discuss with senior physiotherapist. • Oxygen/humidification. • When bleeding has subsided resume treatment as for moderate.

17. Nutrition and Supplemental Feeds

Children with CF have high nutritional requirements, 120-150% of the Estimated Average Requirement (EAR) for energy is considered suitable for most patients.

At each clinic appointment the children are heighted and weighted and BMI plotted on their own centile chart. Babies under one year old should also have their head circumference recorded and plotted. The European CF standards report aiming for a BMI on the 50th centile is ideal.

Poor nutrition or inability to meet nutritional requirements can result in poor lung function, recurrent exacerbations, chronic underlying infection, excessive coughing and gastro disturbances.

In order that the child's high nutritional requirements are met, a high energy, high protein diet should be promoted. Information regarding food fortification is provided. High calorie foods should be encouraged with good nutritional value. Foods with low micro-nutrient value, such as sweets and sugary drinks should not be encouraged as first line as more nourishing foods are available.

If children are unable to meet their nutritional requirements and not following their predicted growth, the following factors should be considered: ensure sufficient calorie intake, ensure PERT (pancreatic enzyme replacement therapy) is optimal, check serum fat soluble vitamin levels, consider CF-related diabetes, other gastro disturbances such as: lactose intolerance, coeliac disease or cow's milk allergy.
To help aid children in achieving optimal nutrition, some children are prescribed nutritional supplements. These drinks are promoted as an addition to the child's normal meals and should not be used as replacement

for food. There is a range of different supplements and children are encouraged to try and range to find the one they find most palatable. Standard oral supplements usually provide 1.5Kcal/ml and are available in 125-200ml bottles.

CF children that are unable to meet their nutritional requirement orally, may require tube feeding. The use of gastronomies in CF has fallen over the recent years, likely due to the early intervention with good nutrition. Naso-Gastric tube (NGT) feeding may be used when unsatisfactory weight gain has occurred. This should be initiated with the agreement of the whole MDT, patient and family. A standard polymeric high energy feed will be used first line and the dietitian will advise on the amount of feed and the rate at which it would be administered. The dietitian will dose the Creon depending on the type and amount of feed used. Creon is usually given (2/3 of the dose) before the feed is started and at the end (1/3 of the dose). Waking children in the night to give Creon is discouraged. The support of the Orchard team will be used with training issues and the patient registered on Homeward to ensure appropriate equipment is available for home use.

Children with CF and their families should be encouraged to make meals times and feeding a positive experience. Children will often go through 'phases' of eating well and not so well. Families should be offered appropriate support to help with the more challenging times. Good nutrition should always be promoted to ensure the child remains as healthy as possible.

During inpatient stays the CF Dietitian will review twice weekly. Patients should be weighed every 3 days, **in light clothes** and **before breakfast**. They should continue normal supplements but may require overnight nasogastric/gastrostomy feeds. A 'CAT number' should be requested at the start of an admission to enable access to high calorie meals and snacks.

18. Chicken pox and CF

Varicella infection can have serious consequences in immunosuppressed children. Special consideration must be given to a CF patient on oral steroids. Firstly check if the child has had significant exposure to chicken pox. Significant exposure is defined as:

a) Being in the same room (e.g. in the house, classroom or dining hall in school) for 15 minutes or more
b) Face to face contact, for example whilst having a conversation during infectious period which is between 48 hours before the onset of the rash until crusting of the lesions

If there has been significant exposure check if there is a previous history of chickenpox or shingles, or if immunity to chickenpox is documented in the notes. In this case no further action needs to be taken. If not, check the antibody status. NB patients with equivocal serological test results should be regarded as NON-IMMUNE.

If the patient is non-immune and is:

1) On a high dose of oral steroids (i.e. 1 mg/kg/day for 1 month or 2 mg/kg/day for 1 week), he/she should have acyclovir prophylaxis for 7 days starting 7 days after exposure to chicken pox
10mg/kg/ dose QDS (max dose 800mg) for 7 days

VZIG* immunoglobulin is currently not recommended unless risk of poor oral absorption or renal impairment and within 7 days of exposure. Need assessment and approval from Public Health England for VZIG

*Dose of VZIG:	0-5 years	250mg
	6-10 years	500mg
	11-14years	750mg

15 years and over 1000mg

2) On a smaller dose or oral steroids, he/she should have aciclovir prophylaxis for 7 days starting 7 days after exposure to chicken pox
10mg/kg/ dose QDS (max dose 800mg) for 7 days

NB children on inhaled steroids are not included in the high risk group.

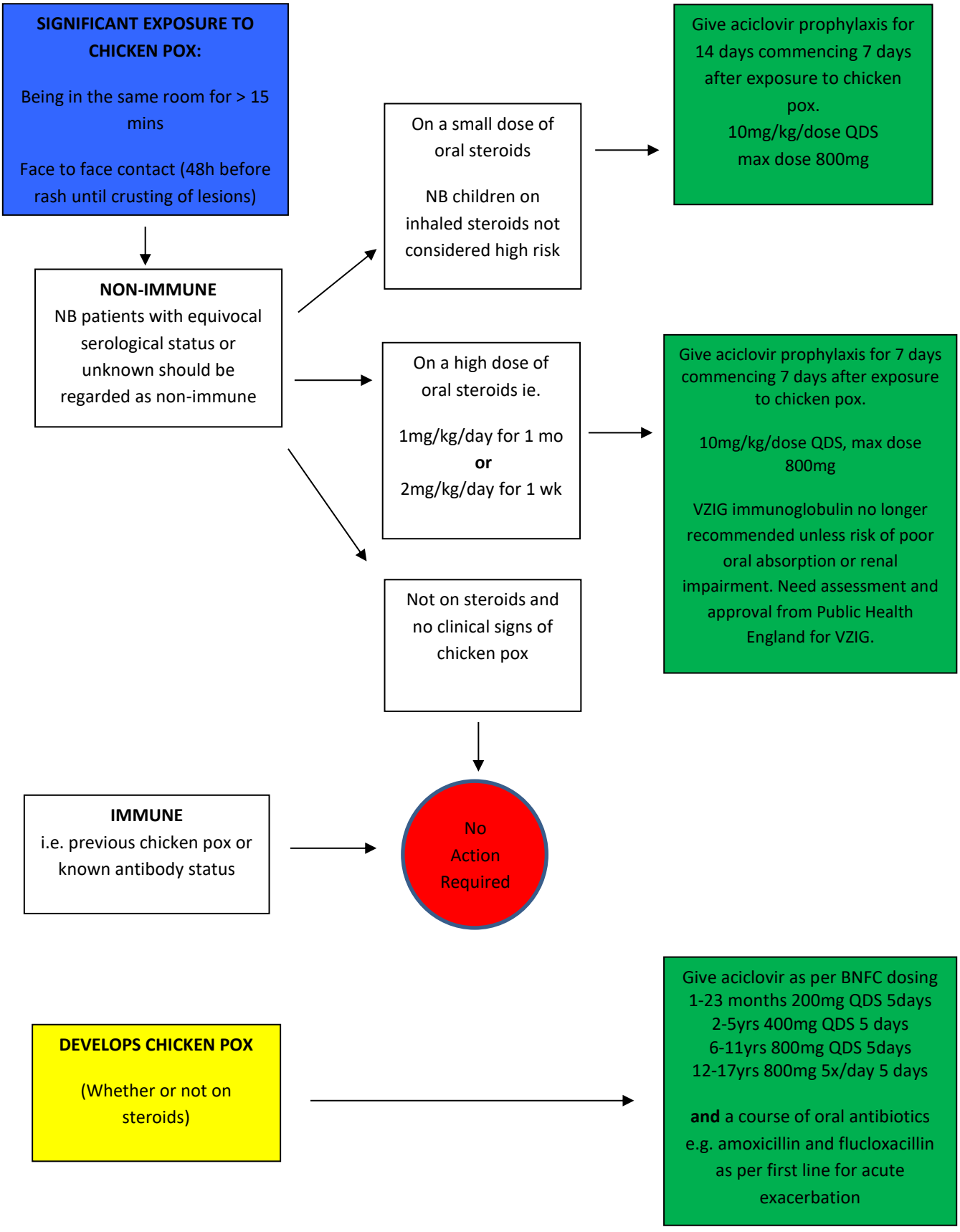
If a child with CF develops chickenpox, give aciclovir as per BNFC dosing

1-23 months	200mg QDS	5days
2-5 yrs	400mg QDS	5 days
6-11 yrs	800mg QDS	5days
12-17 yrs	800mg 5x/day	5 days

and a course of oral antibiotics e.g. amoxicillin and flucloxacillin, as per their usual first line antibiotics for an acute exacerbation.

If a second exposure occurs after 3 weeks, a further dose is required

18.1 Chicken Pox and CF flow chart



19. Meconium Ileus Equivalent (MIE) / Distal Intestinal Obstruction Syndrome (DIOS)

Faeces can accumulate in the distal ileum and caecum causing varying degrees of intestinal obstruction. Children have intermittent abdominal pain, constipation and faecal masses, usually in the right iliac fossa on abdominal palpation. Very mild symptoms may be treated with laxatives (LACTULOSE), encouraging fluids and sometimes adjusting pancreatic enzymes. Otherwise, take the following steps, proceeding from one to the next if the former step fails.

1. LACTULOSE use BNFc dosage
2. ACETYLCYSTEINE: use BNFc dosage
3. MACROGOL (MOVICOL PAEDIATRIC PLAIN) use BNFc dosage
4. KLEAN-PREP can also be considered; usually NG tube needed see BNFc for dose
5. GASTROGRAFFIN*

1- 23 months	15-30ml for 1 dose
> 23 months (15-25kg)	50ml for 1 dose
> 23 months (>26 kg)	100ml for 1 dose

*Note: dose may be repeated after 12-18 hours
encourage drinks/monitor fluid balance (osmotic dehydration) and allow food (NB Gastrograffin has an aniseed flavour)

20. CF and aminoglycosides and hearing

Around 1 in 500 people have the m1555A>G mutation in the mitochondrial gene MT-RNR1 in in the MT-RNR1 gene which is associated with aminoglycoside induced hearing loss. As people with CF are more likely to require aminoglycosides in their lifetime, genetic testing for MT-RNR1 mutations is recommended. This can be done at the same time when other bloods are required.

Patients and families should be counselled of the risk of ototoxicity when prescribed IV aminoglycosides such as tobramycin or amikacin. This risk is increased with dehydration and concomitant use of neurotoxic drugs. This should be clearly documented in the notes (on the CF admission sticker) that this has been explained. Patients should be advised to report any hearing disturbance, including tinnitus.

Additional audiology testing should be requested following a course of aminoglycosides. This can be arranged by email wah-tr.audiologyhearingservices@nhs.net
If the patient is having regular IV aminoglycosides hearing screening should be repeated every 1-2 years.

21. References

1) Birmingham Children's Hospital Department of Cystic Fibrosis and Respiratory Medicine (2019). Guidelines for the Management of Children with Cystic Fibrosis.

2) Royal Brompton and Harefield Hospital NHS Foundation Trust (2023). Clinical Guidelines: Care of Children with Cystic Fibrosis 2023. Available at: https://www.rbht.nhs.uk/childrencf

3) The CF Trust (2011). Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK Available at: https://www.cysticfibrosis.org.uk/~/media/documents/the-work-we-do/care/consensus-docs-with-new-address/cystic-fibrosis-trust-standards-of-care.ashx?la=en

4) Immunisation Against Infectious Disease 'The Green Book' (2017) Available at: http://immunisation.dh.gov.uk/category/the-green-book/ (accessed on 10th January

2013). https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book

5) Cohen-Cymberknoh M, Blau H, Shoseyov D, Mei-Zahav M, Efrati O, Armoni S, Kerem E. Intravenous monthly pulse methylprednisolone treatment for ABPA in patients with cystic fibrosis. J Cyst Fibros. 2009;8:253–7

6) Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis. April 2017 https://www.cysticfibrosis.org.uk/~/media/documents/the-work-we-do/care/consensus-docs-with-new-address/consensus-on-physiotherapy-management-third-edition-2018.ashx?la=en

MONITORING TOOL

This should include realistic goals, timeframes and measurable outcomes.

STANDARDS	%	CLINICAL EXCEPTIONS
Oral antibiotics for patients with cystic fibrosis prescribed according to guideline	100	
Intravenous antibiotics for patients with cystic fibrosis prescribed according to guideline	100	
Cough plate / cough swab or sputum sent at each clinic visit	100	

CONTRIBUTION LIST

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Name	Directorate / Department

Circulated to the chair of the following committee's / groups for comments

Name	Committee / group

Supporting Document 1 - Equality Impact Assessment Tool

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

		Yes/No	Comments
1.	**Does the policy/guidance affect one group less or more favourably than another on the basis of:**		
	Race	No	
	Ethnic origins (including gypsies and travellers)	No	
	Nationality	No	
	Gender	No	
	Culture	No	
	Religion or belief	No	
	Sexual orientation including lesbian, gay and bisexual people	No	
	Age	Yes	For children up to age 18y
2.	**Is there any evidence that some groups are affected differently?**	Yes	Guideline covers only patients up to age of 18y – those over 18y are managed at the adult centre for CF
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	Yes	
4.	**Is the impact of the policy/guidance likely to be negative?**	No	
5.	**If so can the impact be avoided?**	-	
6.	**What alternatives are there to achieving the policy/guidance without the impact?**	-	
7.	**Can we reduce the impact by taking different action?**	-	

If you have identified a potential discriminatory impact of this key document, please refer it to Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact Human Resources.

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	No
2.	Does the implementation of this document require additional revenue	No
3.	Does the implementation of this document require additional manpower	No
4.	Does the implementation of this document release any manpower costs through a change in practice	No
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	No
	Other comments:	

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval

Appendix 1

Cystic Fibrosis Admission Plan **Date:**

- I.V. ceftazidime tds / tobramycin od / other _____ for 2/52
  ☐ Discuss possible side effects of ototoxicity and renal toxicity of tobramycin
  Staff name_____ Signature _____
  ☐ Check aminoglycoside genetics results _____
  ☐ Audiology referral/appt completed
- Nebulised colomycin (million units) bd 2/52 (nebuliser should be changed to colomycin during admission if usually on nebulised tobramycin {bramitob/TOBI}
- Cough plates/ sputum for MC&S (beginning, middle and end of admission)
- Weight beginning, middle and end
- Lung function (beginning, middle and end of admission)
- Overnight continuous SaO2 monitoring first night of admission
- Twice daily physiotherapy including weekends
- CF dietitian to review
- Regular medication to be written up and administered
- TTO's ordered on day 8 (2nd week)
- Check if annual bloods needed

	Admission (date)	Middle (date)	End (date)
Weight kg			
SaO2			
FEV1 (%)			
FVC (%)			
FEF_{25-75} (%)			
Sputum / cough swab			

- 3 post feed BM's within 48 hours of admission (1 hour after food)

	Date/time:	BM
1st		
2nd		
3rd		

Signed:

Appendix 2

Worcestershire NHS Acute Hospitals NHS Trust

DNase Trial Administration Chart

Patient Details: Date:

Consent:

Presenting Condition: ……

Location of trial: ……..

Reason for drug trial: ……..

Current symptoms: ……..

Nebuliser equipment: ……..

Patient completed pre spirometry questionnaire yes/no

Step 1

Baseline spirometry

Pre FEV_1: ……..

Pre FVC:……

FEF $_{25-75}$:……

SaO_2:……..

Step 2

Administer DNase (2.5mg of DNase in 2.5ml)……..

Method of delivery ……..

Record any clinical changes……

Step 3

Repeat spirometry after 30 mins

Post FEV_1: ……

Post FVC: ……

FEF $_{25-75}$:……..

SaO_2:……

% change in FEV_1 ……

% change in FVC ……

Microbiology sent yes/no.

Details:……..……
……
……

Summary of trial and plan:
……
.....
.....
.....

Information given to patient and parents:……

Home delivery: ……

Communication with :……

Signed……..

Assessment of benefit of DNase (guidance only)

18 > 8% relative improvement in FEV_1 and FVC → trial shows benefit and DNase should be continued

19 Fall in FEV_1 or FVC after 4 weeks → DNase should be stopped

20 Suboptimal (<8%) improvement in FEV_1 and FVC but patient reports significant symptomatic benefit → continue the trial for 5 months to allow further assessment of improvement. If assessment after 2 and 3 months fails to show >8% improvement in either FEV_1 or FVC, then DNase should be stopped.

21 Where a patient has had frequent exacerbations requiring IV Abx and the patient feels symptomatic relief without improvement in lung function, a further trial period of 6 months may be appropriate to see if there is a reduction in number of exacerbations.

Appendix 3

Patient Information

Pulmozyme

(Dornase Alpha, DNase)

Pulmozyme is a manmade version of a protein found in your body called DNase. It is also known as DNase, or Dornase Alpha.

How it works:

- It helps to break down the thick mucus found in the lungs of people with CF, and therefore makes it easier to cough up.
- If taken regularly it can help to reduce the number of chest infections and help to maintain or improve your lung function.

How to use it:

The usual dose is one 2.5mg ampoule once a day.

It is important to discuss with your physiotherapist the best time to take Pulmozyme, to ensure you get the maximum benefit from it.

- Do not mix Pulmozyme with any other liquids or medicines in the chamber
- Do not use a nebuliser chamber that has been used for nebulised antibiotics
- Do not use any left over Pulmozyme. This should always be disposed of and the nebuliser pot cleaned after every use.
- Allow at least an hour between taking colomycin and DNase

Preparation:

18 Check the expiry date on the vial (2.5mg)
19 Snap the top off one vial
20 Empty solution into a clean nebuliser chamber
21 Start the nebuliser. Continue until the nebuliser starts spluttering – this indicates that the treatment has finished.
22 If using an e-flow nebuliser continue the treatment until the nebuliser switches off.
23 If using an I-neb make sure you are using a green chamber. You only need to fill the chamber once. The rest must be discarded.
24 After use, clean the nebuliser as directed

When to do your airway clearance (physiotherapy):

- Physiotherapy should be performed at least an hour after taking your DNase.
- A possible routine for your inhaled treatment and physiotherapy may be:

……
……
……

How to store Pulmozyme:

- Pulmozyme can be affected by heat and light so it is important that you store it in a fridge in the original container
- Pulmozyme can still be used if it has been left out at room temperature for no longer than 24 hours.

Side-effects:

Side effects are rare but your child may get one of the following side-effects, usually mild:

- a stomach upset (indigestion)
- fever (temperature above 38°C)
- a sore throat or changes to their voice, such as hoarseness, or temporary voice loss
- a skin rash or sore or irritated eyes (conjunctivitis).

Side-effects you must do something about:

- Rarely, pulmozyme can cause chest pain or increased difficulty with breathing. If these happen contact your doctor straight away.

Appendix 4

Nebulised Hypertonic Saline

Administration Chart

Patient Details: Date:

Consent:

Presenting Condition: ……..

Reason for drug trial:……

Current symptoms: ……

Nebuliser equipment: ……

Location of trial:……..

Patient completed pre spirometry questionnaire yes/no

Step 1

If patient prescribed routine bronchodilators ensure medication taken as normal (have salbutamol if not routine use in case of bronchoconstriction)

Details: ……

Step 2

Baseline spirometry (wait 15 mins if bronchodilators given)

Pre FEV1: ……

Pre FVC:……

SaO2:……..

Auscultation: ……

Step 3

Administer hypertonic saline. Record O2 saturations throughout.

Strength of hypertonic saline and amount ……..

Method of delivery: ……

Record any clinical changes ……

Step 4

Repeat spirometry after 15-20 mins

Post FEV1: ……

Post FVC: ……..

SaO2:……..

Microbiology sent yes/no.

Details:
……
……..

Summary of trial and plan:
……
.....
.....
.....

Information given to patient and parents:……

Repeat prescription:……..……

Communication with :…….

Signed……..

Step 5

Calculate the change in FEV:

$$\frac{\text{(pre FEV1 – post FEV1) x 100}}{\text{Pre FEV}} =$$

Change in FEV1:……%

Routine use of hypertonic saline not recommended if FEV1 drops by 15% from baseline or baseline SaO2 drops by >5% from baseline.

If patient not prescribed routine bronchodilators and trial stopped due to significant drop in FEV1, above may be repeated on separate occasion using pre-test bronchodilator

Appendix 5

Patient Information

Nebulised Hypertonic Saline

Hypertonic Saline is a strong salty sterile solution. Normal saline (sodium chloride) is 0.9% strength whereas hypertonic is either 3%, 6% or 7%.

How it works:

- Hypertonic saline is inhaled into the lungs
- It increases the water content of mucus and makes it less thick and sticky so it is easier to cough up.
- It may lead to an increase in lung function.
- It may reduce the number of chest infections you currently get.

How to use it:

Your physiotherapist/specialist nurse will monitor your response to hypertonic saline the first time you use it to ensure that you have no unwanted side effects i.e. wheeze, chest tightness.

Before using hypertonic saline you should take …….

You will be using hypertonic saline via…….
……
……

25 Check the expiry date on the vial (4mls)
Empty solution into a clean nebuliser chamber:

- **Using an eFlow or conventional compressor**: Empty 4ml of hypertonic saline into your device. Nebulise until there is no more vapour or the machine completes its pre-set delivery.
- **Using an I-neb:** Fill the bubble in the lilac chamber. Nebulise until the I-neb completes its delivery. Immediately refill the lilac chamber from the same vial and inhale a second time to get a full dose.
- When the solution has finished, switch off the nebuliser and rinse nebuliser components in warm soapy water. Leave to dry in air. Because hypertonic saline is a strong salty solution, salt crystals may form in the chamber if it is not washed out after every use.

When to do your airway clearance (physiotherapy):

- Physiotherapy should be performed straight after using your hypertonic saline to maximise the benefits of the solution. Your physiotherapist will advise you which airway clearance technique is most suitable, and how long you should perform it for.

If you have used an airway clearance device (e.g. aerobika) with your hypertonic saline, then you do not need to do additional physiotherapy unless you have been advised otherwise.

How often you should use your Hypertonic Saline:

- When you are well …… times a day
- When you are showing signs of infection or are unwell, ……..times a day

Are there any side effects?

- Nebulised hypertonic saline can make you cough more and bring up more sputum. This is the result we want and it shows that it is working for you.
- Nebulised hypertonic saline can make your airways tight and wheezy. You can usually help to reduce these symptoms by using inhaled or nebulised bronchodilators such as salbutamol
- It can also cause coughing or a hoarse voice.

If you have any these or any other symptoms, please contact the CF team.

Appendix 6

Worcestershire NHS Acute Hospitals NHS Trust

Nebulised Colomycin Administration Chart

Patient Details: Date:

Consent:

Presenting Condition: ……..

Reason for drug trial:…….

Current symptoms: ……

Nebuliser equipment: ……

Location of trial:……..

Patient completed pre spirometry questionnaire yes/no

Step 1

If patient prescribed routine bronchodilators ensure medication taken as normal (have salbutamol if not routine use in case of bronchoconstriction)

Details: ……

Step 2

Baseline spirometry (wait 15 mins if bronchodilators given)

Pre FEV1: ……

Pre FVC:……

SaO2:……

Auscultation: ……

Step 3

Administer colomycin. Record O2 saturations throughout.

Strength of colomycin and amount……..

Method of delivery: ……

Record any clinical changes ……

Step 4

Repeat spirometry after administration:

Post FEV1: ……

Post FVC: ……..

SaO2:……..

Microbiology sent yes/no. Details:
……
……..

Summary of trial and plan:
……
.....
.....
.....

Information given to patient and parents:…….

Repeat prescription:……

Communication with :…….

Signed……..

Appendix 7

Patient Information

Nebulised Colistimethate Sodium

(Colomycin)

What is Colomycin?

Colomycin is an antibiotic that is used to treat a number of infections.

What is Pseudomonas?

Pseudomonas is a bacterium that lives in soil, water, and warm environments and is generally all around us. For healthy individuals this does not cause a problem, for those with Cystic Fibrosis (CF) it can cause infections in the lungs. Most young people with CF do get pseudomonas at some stage and it is possible to get rid of this initially by antibiotic treatment. It is unlikely that there is anything you have done/not done that would have caused it.

What is a nebuliser?

A nebuliser is a piece of equipment that enables medication to be inhaled as a mist. The fine mist allows particles to be breathed in efficiently to reach the small airways of the lungs. The team will provide you with the most appropriate nebuliser for you/your child and show you how to use it and look after it.

Are there any possible side-effects?

The first time you have inhaled antibiotics you will be monitored in clinic. If any chest tightness/wheeze is experienced, we may give another inhaled medication called salbutamol to help you take the inhaled antibiotic.

How long will the treatment continue for?

The inhaled antibiotic is usually continued for 3 months, alongside an oral antibiotic, or I.V. antibiotics (given into a vein).

The colomycin dose can vary and will be prescribed by your consultant.

The treatment may continue long-term if you continue to grow pseudomonas.

The dose you have been prescribed is:

_____

How do I give the medicine?

The first dose will always be given in hospital, as prescribed by your consultant.

For all other doses you will need to mix the medicine as follows:

- Wash your hands
- Always check the use by date of the medicine
- Flip open the plastic cap

- Carefully rip the foil seal from around the top of the vial
- Remove the rubber bung
- Add 2-4mls sodium chloride (0.9% saline) into the bottle of colomycin either with a syringe or measured into a medicine pot. Water for injections can be used instead of saline.
- Slowly and carefully mix the solution . DO NOT shake vigorously as this creates a lot of bubbles and the medicine takes a lot longer to dissolve.
- Pour the solution into the nebuliser once the liquid is clear. (use the grey chamber with an I-neb)
- Colomycin should be used immediately after it has been prepared.

When should the nebuliser be given?

Ideally nebulised antibiotics should be given with no-one else in the room where possible, although this is not always practical.

Ensuring the room is well ventilated by opening a window, or by using elephant tubing to filter it out of the room can reduce the amount of medication inhaled by anyone else.

Colomycin is best taken after a physiotherapy session to ensure that the medicine stays in the lungs as much as possible.

If you are taking DNase, please remember to allow 1.5 – 2 hours between colomycin and your DNase.

Frequently asked questions:

- ***How long will the nebuliser take?***

  The nebuliser will take 5-15 minutes depending on the type of nebuliser unit you have.

- ***Do I need to do more regular cough swabs?***

  Yes, you will need cough swabs monthly for the next 3 months. This will be arranged by the specialist nurse or physiotherapist.

- ***What if I accidentally miss a dose?***

  Take the dose as soon as you remember, unless it is near the time for the next dose. You do not need to make up for the dose you have missed.

· Are there any other side-effects to taking colomycin?

As with all medicines, colomycin can cause side effects although not everyone gets them. If you develop a tight chest, wheeze or difficulty breathing then take your usual ventolin (Salbutamol) and contact your GP urgently. If this does not improve with Salbutamol, go to the Accident and Emergency Department at your local hospital.

Colomycin can cause allergic reactions like skin rash—if this happens stop taking colomycin and contact the CF team. Colomycin can cause a sore throat or sore mouth so rinsing your mouth after nebulisation is advised.

Appendix 8

Secretary contact telephone numbers	
Dr N Ahmad and Dr C Onyon	**01527 503030 ext 44121**
Dr T Dawson and Dr W Shinwari	01527 503892
Dr K Nathavitharana	01562 828886
Dr L Harry and Dr T Bindal	01562 828804
Dr A Short	01527 503030 ext 44927
Dr A Gallagher and Dr V Weckemann	01905 760662
Dr J West	01905 733972
Dr M Hanlon and Dr M Ahmed	01905 760734
Dr B Kamalarajan	01905 760736
Dr P van der Velde	01905 733882

Department of Paediatrics

Worcestershire Royal Hospital
Charles Hastings Way
Worcester
Worcestershire
WR5 1DD

Outpatient clinic Alex 01527 512758
Outpatient clinic WRH 01905 733476
Outpatient clinic KTC 01562 823424 ext 55174

Dear Dr

During hot weather, children with cystic fibrosis (CF) lose more salt in their sweat. This can lead to lethargy and cramp.

We recommend that children with CF go onto salt supplements in the hot weather (when the outside temperature is over 18-20 °C). In children aged less than 1 year it may be given all through the year.

For children who can swallow tablets/capsules, we recommend SLOW SODIUM tablets (600 mgs =10 mmol Na)

The dosage is according to age: (delete as appropriate):

2 to 5 years:	Slow Sodium tablets (600 mg) one tablet once (to twice) a day
5 to 10 years:	Slow Sodium Tablets (600 mg) one tablet once to twice daily
10 years & over:	Slow Sodium Tablets (600 mg) one tablet twice to three times a day

For babies and young children who are unable to swallow tablets, will need SALT SOLUTION (1mmol/ml, 1mmol=58.5mg Na):

Below 2 years:	2 mmol/kg/day in 2 or more divided doses (Maximum dose 20mmol per day)
2 to 5 years:	1 mmol/kg/day in 2 or more divided doses (Maximum dose 20mmol per day)

Please do not hesitate to contact us if you have any questions.

With many thanks for your help.

Yours sincerely

Dr Clare Onyon
MA(Cantab) MA(MedEd) MB BChir(Cantab) MRCPCH
Consultant Paediatrician

Appendix 9

NHS Birmingham Women's and Children's NHS Foundation Trust

RESPIRATORY AND CYSTIC FIBROSIS UNIT

Dr Ben Davies – Consultant Respiratory Paediatrician
Dr Maya Desai – Consultant Respiratory Paediatrician
Dr Satish Rao – Consultant Respiratory Paediatrician
Dr Priti Kenia - Consultant Respiratory Paediatrician
Dr Isobel Brookes - Consultant Respiratory Paediatrician
Dr Prasad Nagakumar - Consultant Respiratory Paediatrician

DEPARTMENT TEL: (0121) 333 8199 / 8202 / 8205 Tel: 0121 333 9999

This form can be sent to: bwc.bchcfadmin@nhs.net

CN score request form

Shared care centre: Worcester Royal Hospital

Name of patient: _____

NHS No (mandatory): _____

BCH Hosp No (mandatory) _____

Date of birth: _____

Date of Chest x-ray*: _____

Date sent: _____

Requested by
(please print name and sign): _____

CN score given: _____

Scored by

(please print name and sign):_____

Please return completed score to: maya.desai@nhs.net for review and dissemination