LRI Children's Hospital

Prescribing in Cystic Fibrosis

Staff relevant to:	Clinical staff working within the UHL Children's Hospital.
Team approval date:	April 2023
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Written by: Reviewed by:	S Popple V Pankhania
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1. Introduction and Who Guideline applies to

This guideline should be used in conjunction with the cystic fibrosis inpatient guideline and the injectable medicines guide for children.
The purpose of this guideline is to provide practical information to aid prescribing for this complex group of patients.

Related documents;

Cystic Fibrosis Related Diabetes UHL Childrens Hospital Guideline C9/2018

Cystic Fibrosis Emergencies UHL Childrens Medical Guidelines C64/2015

Cystic Fibrosis Outpatient Care UHL Childrens Medical Guideline C38/2016

Cystic Fibrosis - Inpatient Chest Exacerbation UHL Childrens Medical Guideline C36/2016

Anaphylaxis UHL Paediatric Emergency Department Guideline B18/2019

Contents

2. CF Treatments

2.1 Antibiotic Treatment.

- Cystic fibrosis patients in general need higher doses of antibiotics for a longer duration (10-14days) than other children due to increased clearance and volume of distribution. Severe infection doses are usually used.

- **Dual** therapy should be used when treating *Pseudomonas aeruginosa* to limit emergence of resistance. Beta lactam antibiotics (cephalosporins, carbapenems, Tazocin) and aminoglycosides are considered to be synergistic.

- For dosing and monitoring information of individual drugs please see the Paediatric Cystic Fibrosis Drug Formulary in the links below;
  For intravenous (IV) drugs click here
  http://insitetogether.xuhl-tr.nhs.uk/SP2007/Pharmacy/CF%20IV%20DRUG%20FORMULARY%20FINAL%20NOV%202018.pdf

  For oral (PO) drugs click here
  http://insitetogether.xuhl-tr.nhs.uk/SP2007/Pharmacy/CF%20ORAL%20DRUG%20FORMULARY%20FINAL%20NOV%202018.pdf

  For nebulised drugs click here
  http://insitetogether.xuhl-tr.nhs.uk/SP2007/Pharmacy/CF%20INHALED%20DRUG%20FORMULARY%20FINAL%20Feb%202019.pdf

- Allergy status **must** always be confirmed and documented clearly in line with the NICE drug allergy guideline before prescribing.

- Choice of antibiotics will usually be previously determined by the CF multidisciplinary team with input from a Consultant Microbiologist. Micro codes may still be required for certain agents. Please check the antimicrobial website.

- Prescribe clearly on inpatient chart including flushes / heparin lock for IV antibiotics.
    - Sodium Chloride 0.9% 10ml after each antibiotic
    - Heparin Saline 10units/ml
    - Heparin Saline 100units/ml 4ml for portacaths*

* care with strength of heparin in younger patients as three times daily exposure of heparin may approach 1/4 of an anticoagulant dose in patients <12kg . If necessary use a smaller volume or 10units/ml.

- All patients with a long line or accessed portacath should receive the appropriate MRSA decolonisation regimen as an inpatient. Yellow stickers are available on the wards to facilitate prescribing.

- Nebulised aminoglycosides (tobramycin / amikacin) should not be administered concurrently with intravenous aminoglycosides.

- Colistin (Colomycin® / Promixin®) is also stopped on most occasions to give a break from treatment while on IV therapy but the CF team may decide to continue it in some patients. It should not be continued if the patient is to receive intravenous colistin.

- Patients receiving aminoglycosides or Ambisome (antifungal) must be adequately hydrated. Consider IV fluids if vomiting, diarrhoea, or inadequate intake.

- Prophylactic oral antibiotics (usually BD flucloxacillin, BD co-amoxiclav or 3x weekly azithromycin) are also stopped for the duration of IV course. Macrolides and ciprofloxacin in NTM patients are continued as part of the treatment regimen. Ensure they are re-started at the end of treatment and stated on the discharge letter for GP to continue.

First line IV antibiotics:

- For younger patients who have not isolated *Pseudomonas aeruginosa* in the previous 2 years, cefuroxime may be used as monotherapy unless cultures and sensitivities indicate otherwise. This broad spectrum antibiotic will cover the main pathogens found in younger cystic fibrosis patients including Streptococcus, methicillin-sensitive S*taphylococcus* and Haemophilus influenza.

Patients who isolate *Pseudomonas aeruginosa*:

- Our usual combination of antibiotics for patients who have isolated *Pseudomonas aeruginosa* in the previous year, or who are known to be colonised, is ceftazidime IV + tobramycin IV.

- For patients that have also recently isolated, or have a repeated history of isolating methicillin-sensitive *Staphylococcus aureus*, additional oral flucloxacillin may be prescribed or ceftazidime replaced with either Tazocin or meropenem. This will depend on known sensitivities and allergy status.

Non-Tuberculous Mycobacterium (NTM)

- Patients with non-tuberculous mycobacterium (NTM) will receive an intensive regimen with a combination of 4-5 drugs both IV and oral for a duration of 3 weeks under specialist advice.

- Treatment is for a duration of 3 weeks therefore be mindful of administration times to ensure patients get adequate sleep. Also aim to give drugs consecutively to limit number of times the line / port is accessed and number of heparin flushes per day.

- Consideration should be given to the emetogenicity of these regimens, particularly those including tigecycline or imipenem, and appropriate antiemetics such as aprepitant prescribed (see CF oral drug formulary).

Home IV Antibiotic Prescriptions

- Some patients will go home for all or part of their 2 week course of antibiotics at the discretion of the CF team.

- The first dose of all courses **must** be administered in hospital. Patients should usually stay for 48 hours to ensure full review by the multidisciplinary team.

- Patients will have pre-made antibiotics delivered via homecare. On occasions where parents/ carers are trained it may be appropriate to send home with vials. This is at the discretion of the CF team.

- Homecare is co-ordinated by the CF team and paediatric pharmacy team.

- All patients will require a full TTO on ICE. All antibiotics and flushes should be prescribed and source selected as homecare or pharmacy.

- Ensure that 'other medications as on admission' is also indicated on the TTO to avoid regular medications being removed from the patients repeat prescription. Ideally they should be prescribed in full.

- All patients should be issued with one adrenaline pen (Epipen® or Jext®) prescribed as 'in case of anaphylaxis'. Patients may have been issued one recently for a previous course of IVs. Confirm with parent / carer that they still have it and ensure they have checked the expiry. Training is nurse led for new patients and should be regularly refreshed ensuring the correct device is used.

- Body weight:

<31kg	Jext 150 micrograms
≥31 kg	Jext 300 micrograms

OR

< 26kg	Epipen 150micrograms
≥ 26kg	Epipen 300 micrograms

For those receiving vials ensure the following is prescribed;

- Antibiotic ampoules or vials
- Appropriate reconstitution solution (see IV administration guide / pharmacist)
- Appropriate diluent if infusion necessary (see IV administration guide / pharmacist)
- Flush for long line / portacath.
    - Heparin Sodium 100 units / ml for ports 4ml flush *
    - Heparin Sodium 10 units / ml for longline 2-4ml flush
    - Sodium Chloride 0.9% (ports and lines) 10ml flush

  *see note above regarding 100units/ml heparin in younger patients.

Dispensing these items is time consuming for pharmacy. Please inform the CF pharmacist / paediatric pharmacy team as soon as possible of patients who are going home on IVs so that a supply can be made in a timely manner. Full instructions on reconstitution, drawing up dose and administration must be provided by pharmacy and competence confirmed by CF nurse.

2.2 CFTR Modulators

Increasingly patients with CF will be on CFTR (Cystic Fibrosis Transmembrane conductance Regulator) modulators depending on their underlying genotype. These are;

- Orkambi (Lumacaftor/Ivacaftor),
- Symkevi (Tezacaftor/Ivacaftor),
- Kaftrio (Elexacaftor/Tezacaftor/Ivacaftor)
- Kalydeco (Ivacaftor) prescribed with Symkevi and Kaftrio as evening dose or as monotherapy for certain genotypes.

- CFTR Modulators should be continued in all patients unless NBM or unable to tolerate oral medications.
- Patient's own supply must always be used. Supplies are made on an outpatient repeat basis via LRI Trustmed.
- Modulator doses should be taken as close to 12hours apart as possible with a fat containing food or snack (6-8g fat) with Creon for those with pancreatic insufficiency.
- CFTR modulators have complex drug-drug interaction profiles, please **see oral drug formulary and manufacturer's specification of product characteristics (SPC) for further information** and ensure drug interactions are checked for all newly prescribed drugs. Particular care with all drugs which inhibit or induce cytochrome P450 enzymes. This includes **clarithromycin, azole antifungals, aprepitant** and many more drugs. Main mechanisms for interactions involve CYP3A4&5, CYP2C9 and p-glycoprotein and vary with each modulator combination.

2.3 Nebulised Drugs

Antibiotics

- All first doses should be given in hospital with pre and post spirometry to assess for bronchospasm
- Always give nebulised antibiotics AFTER physio.
- Stop nebulised aminoglycosides during admission in patients receiving IV aminoglycosides (see above)
- Nebulised colistin (Colomycin/Promixin) may be continued at the discretion of the CF team but is often stopped to allow for a break or other inhaled agents.
- Promixin is only administered via the I-neb (patient's own) in the grey chamber.
- Bramitob (tobramycin) may be administered via the I-neb in the lilac chamber only and nebulised twice consecutively per 300mg dose. If also on hypertonic saline, a second lilac chamber is required.

Mucolytics

- DNase (Dornase alfa/Pulmozyme) should be given 1 hour prior to chest physiotherapy, or last thing before bed.
- Usually prescribed at 12pm as an inpatient to fall between twice daily physiotherapy sessions
- DNase can be administered as 1ml via the I-neb in the green chamber.
- Hypertonic saline (sodium chloride) 3-7% may be prescribed PRN to aid mucus clearance.
- In younger patients or those intolerant of hypertonic solutions, 0.9% may be used.
- Ensure salbutamol inhaler is prescribed PRN. Pre-treat hypertonic saline with 4-6 puffs salbutamol as bronchospasm is common.
- Hypertonic saline can be administered via the I-neb as a 1ml dose nebulised twice consecutively (using lilac chamber). A second lilac chamber is required for patients also on Bramitob.

2.4 Vitamins, Pancreatic Enzymes, Nutritional Supplements

- Should all be prescribed on inpatient chart
- Patients who are pancreatic insufficient are usually on vitamins ADE and K as Paravit CF liquid or capsules. Check dose with patient / carer. Levels are checked at annual review and amendments to regimen made as necessary.
- Creon 10,000 and Creon micro for younger patients are most used.
- Creon 25,000 generally used in older patients
- Prescribe PRN for meals and snacks, no maximum.
- Pancrex V powder may be used in patients for NG or PEG administration.
- Patients must have access to these in their room.
- See oral drug formulary for further information

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Adherence to outlined prescription requirements	Retrospective or prospective review of TTOs and drug charts	Senior Pharmacist Paediatrics	Every 4 years	Local clinical practice group and Q&S lead

5. Supporting References

- NICE guideline ng78 Cystic Fibrosis; diagnosis and management. October 2017
- Report of the UK Cystic Fibrosis Trust Antibiotic Working Group; 3rd edition accessed April 22
- Nutritional management of CF 2nd edition accessed April 22
- BNF for children. Online version accessed April 22
- http://www.medicines.org.uk – Specifications of Product Characteristics – accessed April 22.
- Clinical Commissioning Policy; Inhaled Therapy for Adults and Children with Cystic Fibrosis Dec 14. NHS England A01/P/b
- NICE guideline [CG183] Drug allergy: diagnosis and management. September 2014.

6. Key Words

Antibiotics**,** Cystic Fibrosis Transmembrane conductance Regulator, Mucolytics, Nutritional supplements, Pancreatic enzymes, Vitamins

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details	
Guideline Lead (Name and Title) Sarah Popple - Advanced Pharmacist Practitioner - Children's Respiratory Medicine Vandana Pankhania- Advanced Specialist Pharmacist Paediatrics	**Executive Lead :** **Chief Nurse**

November 2022 – April 2023: Details of Changes made during review

Following added:
Page 2:

- Cystic fibrosis patients in general need higher doses of antibiotics for a longer duration (10-14days) than other children due to increased clearance and volume of distribution. Severe infection doses are usually used.
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- Micro codes may still be required for certain agents. Please check the antimicrobial website.

Page 3:

- Patients receiving aminoglycosides or Ambisome (antifungal) must be adequately hydrated. Consider IV fluids if vomiting, diarrhoea, or inadequate intake.
- Ensure they are re-started at the end of treatment and stated on the discharge letter for GP to continue.

Page 4:

- Added dosing of Jext and Epipen

Page 5:

- Full instructions on reconstitution, drawing up dose and administration must be provided by pharmacy and competence confirmed by CF nurse.
- CFTR modulator information.

Page 6:

- Bramitob (tobramycin) may be administered via the I-neb in the lilac chamber only and nebulised twice consecutively per 300mg dose. If also on hypertonic saline, a second lilac chamber is required.
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Page 7:

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- Patients must have access to these in their room

Following Removed:
Page 2:

- Allergy status **must** always be confirmed and documented before prescribing including the nature of the reaction as per the UHL Allergy Policy. Removed note referring to policy as it no longer exists.

Page 3:

- Please note that meropenem is not available as a pre-made antibiotic from homecare

Page 4:

- Dosing for generic adrenaline pen removed as dose varies with brand of pen.

Page 6:

- Hypertonic saline (sodium chloride) 3.5-7% may be prescribed PRN to aid mucus clearance during inpatient stays

Page 7:

- Patients are usually on Vitamins A+D (Dalivit for younger pts) and Vitamin E (alpha tocopheryl) capsules (75 unit) / suspension (1mg/ml). Check dose with patient / carer.