SHARED CARE PRESCRIBING GUIDELINE
Nebulised mucolytic and antibiotic solutions for the treatment of Cystic Fibrosis in existing paediatric patients only (i.e. those who are <18 years of age and are historically being prescribed these medicines in primary care)

Nebulised mucolytic and antibiotic solutions for the treatment of Cystic Fibrosis in paediatric patients NOTES to the GP

The information in the shared care guideline has been developed in consultation with CCGs in South East London and it has been agreed that it is suitable for shared care.

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing **nebulised mucolytic and antibiotic solutions** for the treatment of **Cystic Fibrosis (CF).**

Due to the planned repatriation of nebulised therapies, shared care is not appropriate for newly diagnosed patients or patients that are newly transferred to the King's College Hospital paediatric Cystic Fibrosis service. Therefore, this shared care guideline only covers existing patients who are already being prescribed such therapies in primary care by their GP.

The questions below will help you confirm this:

- Is the patient's condition predictable or stable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.

If the answer is NO to any of these questions you should contact the requesting consultant or your local CCG Medicines Management Team. There may be implications for the patient where the invitation to share care is declined. For example, the patient may need to be changed to an alternative treatment regimen. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **It is important that patients are consulted about treatment and are in agreement with it**.

Prescribing should follow requirements in the South East London Interface Prescribing Policy.
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount.

Once you have read the shared care guideline and considered the information above, please complete the GP decision form on the next page and email back to the requesting clinician if you are in agreement to participate in shared care.

Nebulised mucolytic and antibiotic solutions for the treatment of existing paediatric patients with Cystic Fibrosis only (i.e. those who are <18 years of age those and are historically being prescribed these medicines in primary care)

This shared care guideline covers the prescribing of dornase alfa, colistimethate sodium, tobramycin and aztreonam lysine nebuliser solutions, to aid sputum expectoration and/or for paediatric CF patients either newly colonised with Pseudomonas aeruginosa for eradication therapy or long-term therapy in those who are chronically colonised.

Sputum expectoration

There is an intense inflammatory response to chronic bacterial infections in the lungs of people with CF, which results in the release of large amounts of DNA from nuclei of disintegrating neutrophils in the airways. The DNA polymerises with glycoproteins and increases the viscosity of the sputum, making it difficult to expectorate. DNase is a naturally occurring enzyme which hydrolyses extracellular DNA. Recombinant human DNAse (dornase alfa or Pulmozyme®) has been shown to reduce viscoelasticity of CF sputum, aiding sputum expectoration resulting in improved lung function and reduced frequency and severity of pulmonary infective exacerbations in patients with CF. The main aims of clinical use are to optimise lung function and reduce the frequency of respiratory infections.

Pseudomonas aeruginosa eradication

The success of early identification and treatment in preventing Pseudomonas aeruginosa infections becoming established and chronic, frequently determines a patient's future quality of life and long-term survival. Patients who are newly colonised with Pseudomonas aeruginosa will undergo an eradication regimen involving nebulised antibiotics thus avoiding the establishment of chronic infection.

Nebulised tobramycin and colistimethate sodium (Colomycin® or Promixin® powder for nebuliser solution brand only. Promixin® powder for nebuliser solution is prescribed for patients who have an I-neb® nebuliser device) are antibiotics licensed for the treatment of Pseudomonas aeruginosa lung infections in patients with CF.

In paediatric patients at King's College Hospital first line treatment for eradication of Pseudomonas aeruginosa is a 3 week course of ciprofloxacin and a 3 month course of nebulised colistimethate sodium. The duration of either is extended according to individual patient's progress. Intravenous antibiotics or one month (or more) of nebulised tobramycin may be used if the child becomes unwell or if Pseudomonas is re-isolated despite the first line treatment.

Eradication therapy may be repeated if previous attempts were unsuccessful.

Chronic Pseudomonas aeruginosa colonisation

In patients chronically infected with Pseudomonas aeruginosa, regular nebulised antibiotics reduce the rate of deterioration of respiratory function. Studies of the potential benefits of nebulised antibiotics in patients with chronic Pseudomonas aeruginosa infections have demonstrated improved lung function, a slower decline in lung function and fewer hospital admissions. Therefore long term nebulised anti-pseudomonal antibiotics are frequently used in the treatment of CF patients who are chronically colonised.

A stepwise approach to prescribing is recommended.

- Colistimethate sodium nebules (Colomycin® Injection (licensed for inhalation) or Promixin® Powder for Nebuliser Solution) are used first line when pulmonary function is normal but chronic Pseudomonas aeruginosa infection is evident.
- Tobramycin nebules should be considered if, despite continued therapy and good adherence to treatment, lung function continues to decline or there is a requirement for more than one course of IV antibiotics in the preceding year.
- Aztreonam lysine nebules (Cayston®) may be considered if there is still progressive loss of lung function (defined as greater than 2% per year decline in FEV1 as % of predicted) or there is continued need for IV therapy for exacerbations i.e. more than 2 per year despite therapy with an alternating regimen of Colistimethate sodium and tobramycin. Aztreonam is licensed for patients aged 6 years and above.

Nebulised antibiotics can be given as a continuous daily suppressive regime (colistimethate sodium only), on a month on/month off basis, or alternating monthly with an alternative antibiotic. All of the nebulisers above are commissioned by NHSE

CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- Prescribing responsibility will only be transferred when the consultant and the GP are in agreement that the patient's condition is stable or predictable and once the patient is established on therapy.
- Prescribing by the GP will only be transferred once the GP has agreed each individual case. King's College Hospital will continue to provide prescriptions until there has been successful transfer of responsibilities outlined below.
- **Note:** There is no "GP decision form" included in this guideline, which is usually used to confirm acceptance from the GP to take over prescribing from the hospital for new patients. This document aims to guide and support primary care prescribers who are **already** prescribing in this setting. The transfer of new patients to primary care is **not** included within the scope of this shared care guideline.

AREAS OF RESPONSIBILITY

Consultant / Specialist team

- Assess patient and establish need and suitability for nebulised therapy.
- Baseline monitoring of lung function (FEV_1), weight, oxygen saturation, renal function and symptoms. Sputum microbiology cultures will be taken as routine.
- Prior to initiation of antibiotic nebuliser solutions, administer a test dose under hospital supervision due to the risk of bronchospasm . One dose of the intended nebuliser solution should be given, using a pre-nebulisation bronchodilator if this is part of the current regimen for the patient. FEV_1 should be measured before and after nebulisation. If there is evidence of therapy-induced bronchospasm in a patient not receiving a bronchodilator the test should be repeated, on a separate occasion, using a bronchodilator. If bronchoconstriction is <10%, the patient is suitable for treatment.
- To initiate, stabilise and supply treatment (including diluents) for the first 1 month and where necessary refer to the CF physiotherapist for supply of a suitable nebuliser device.
- To inform patients of practical issues related to the use of their nebuliser solution such as training on use of nebuliser, reconstitution (if applicable), administration, storage and who to contact if they experience problems with nebuliser equipment.
- Discuss treatment with patient and ensure they have a clear understanding of it.
- Specify the brand of nebulised therapy and provide reconstitution information where applicable, to both the patient and the GP.
- Provide patient with a patient information leaflet (ensuring brand specific where applicable)
- At the time of initiating, notify GP in writing that the nebuliser solution has been prescribed. The GP should be invited to share care once the patient is stable. Information provided to the GP should include:
    - A copy of the shared care guidelines
    - The specific brand of nebulised therapy to be prescribed (where applicable)
    - That a prescription for the first 1 month supply has been given
    - Information on when the patient will next be reviewed and by whom
    - A request that the GP continue prescribing after 1 month
    - Indication and expected treatment duration
    - Information detailing that monitoring will be undertaken by the Specialist center
- Monitor patient's continuing response and need for therapy at month 1 and month 3 and send letter to GP following clinic.
- Continue to monitor urea, electrolytes, renal function, lung function (FEV_1), and sputum microbiology 3 monthly and send letter to GP following clinic.
- To review patient at the request of GP should any problems arise (e.g. side-effects / lack of efficacy). The patient must be reviewed within 1 month of problems arising according to clinical necessity.
- To communicate promptly (within 2 weeks) with the GP if treatment is changed or if any abnormal monitoring results are found; it is the responsibility of the Consultant/ Specialist team to undertake any action relating to an abnormal result being reported.
- To report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk

General Practitioner responsibilities

Before agreement to shared care:

- To consider shared care proposal within 2 weeks of receipt. If agree to request to continue prescribing as detailed in shared care guideline confirmation to the requesting CF consultant is required **within 2 weeks** of receipt of this guideline by completing and returning the agreement on page 2.
- If named GP not available within 2 week time-frame to pass to a GP colleague for consideration.
- If do not agree to shared care, discuss with requesting CF consultant or local primary care CCG medicines management team within 2 weeks of receipt of shared care request.

After agreement to shared care:

- To provide ongoing prescriptions for the nebuliser solution initiated after 1 month, prescribed by brand where specified as brands are not interchangeable.
- To provide ongoing prescriptions for sodium chloride 0.9% and/or water for injections in order to reconstitute Promixin® and Colomycin® if applicable and as specified by the CF Team at King's College Hospital; to provide sharps containers for waste disposal.
- To agree to the GP monitoring requirements of this document.
- To seek advice or report any concerns (e.g. side-effects, co-morbidities, pregnancy, lack of efficacy) by contacting the relevant CF team member (contact details listed on page 13). To discuss with CF team before discontinuing treatment.
- To encourage adherence to prescribed treatment and to advise specialist team if non-adherence is suspected.
- To refer back to CF team if the patient's condition deteriorates.
- To check for drug interactions when prescribing new or stopping existing medications.
- To stop treatment on the advice of the CF team or immediately if an urgent need to stop treatment arises.
- To discuss unmanageable problems with the CF team, so that if necessary, prescribing responsibility can be transferred to the CF team.
- To report any suspected adverse effects to the MHRA via the Yellow Card scheme:: http://www.yellowcard.gov.uk

Patient's / Parent/ Carer's responsibilities

- To contact the CF team if he or she does not have a clear understanding of any aspect of the treatment.
- To contact the CF team if any problems are experienced with administration or if any equipment is required.
- To inform their community pharmacy of the new medication to minimise delays in obtaining treatment.
- To inform CF consultant, GP and other healthcare professionals of any other medication (new or existing) being taken, including, over the counter products, alternative therapies or recreational drugs.
- To inform community pharmacists of the medication that they take before purchasing medication over-the-counter.
- To attend all hospital and GP appointments; if unable to attend a scheduled hospital/ GP appointment the hospital/ GP should be informed and the appointment re-scheduled.
- To take medicines as agreed and take steps to ensure that no doses are missed and not to share medicines with others.
- To read the patient information leaflet included with the medication and discuss any concerns with the CF team, your GP or community pharmacist if you need any more information to help you take your medicine as prescribed.
- To report any adverse effects or warning symptoms to GP or CF team.
- To report to GP and CF team if pregnant or breastfeeding (female patients only).
- To inform GP and hospital of any changes in addresses or telephone contact numbers.
- Ensure you have adequate supplies and knowledge of appropriate storage of medications before going on holiday in the UK or when travelling abroad.

Information provided to the patient by the Specialist Team

- Discuss treatment with patient and ensure they have a clear understanding of the dose and frequency.
- Ensure the brand of nebulised solution that the patient has been successfully trialled with is specified to the patient and the importance of not switching brand emphasised.
- Patient provided with a Patient Information Leaflet (PIL) of the nebuliser solution prescribed.

There should be a gap of at least 30-60 minutes between administering dornase alfa and administering a nebulised antibiotic, as the latter will denature dornase alfa.

Patients informed of practical issues related to the use of nebuliser solutions:

- Reconstitution instructions (if applicable)
- Storage instructions
- After each use the nebuliser chamber should be washed with a mild detergent solution, rinsed thoroughly and allowed to dry naturally before reassembly
- A minimum weekly sterilisation is recommended, ideally after each use (follow manufacturers advice)
- Who to contact if they experience problems with the nebuliser equipment

Monitoring Information

NOTE: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for the respective nebulised therapies prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk).

Dornase Alfa

Dose, Route of Administration and Duration of Treatment	Monitoring Undertaken by Specialist Requesting Shared Care	Ongoing Monitoring to be Undertaken by GP	Stopping Criteria	Follow Up
2.5 mg (2500 units) nebulised once daily. **Duration of Treatment** Indefinite	**Baseline** Lung function (FEV_1), weight, oxygen saturation and symptoms **In paediatric patients:** Lung function (FEV_1) is taken pre and post the first test dose to check for excessive bronchoconstriction and/or wheeze to ensure suitability of the drug **Assessment of response** Initial response will be assessed at months 1 and 3, with a repeat of lung function (FEV_1), weight, oxygen saturation and symptoms	No routine monitoring is necessary Report any concerns about side-effects, pregnancy, overuse, poor adherence or lack of efficacy to the CF team Report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk	No changes should be made to treatment without prior discussion with the CF team Response to treatment will be assessed on an individual basis by the CF consultant. Treatment will be discontinued in patients whose lung function has deteriorated after the trial period (1-3 months depending on the severity of disease). Intolerable adverse effects would necessitate withdrawal **Note** - Patients who discontinue dornase alfa may be considered for a repeat trial in the future	**Specialist** Patients monitored 3 monthly (lung function (FEV_1), weight, oxygen saturation and symptoms Send a letter/results notification to the GP after each clinic attendance Advise GP on review, duration and/or discontinuation of treatment where necessary **GP** To follow up as required at discretion of GP Request patient seen earlier if adverse effects experienced between appointments

Practical issues including adverse effects, interactions, other relevant advice and information (refer to BNF for full list)

1. **Adverse effects** – Dysphonia, pharyngitis, laryngitis, dyspnoea, non-cardiac chest pain, pyrexia, conjunctivitis, dyspepsia, rash, urticarial (rare < 1/ 1000). Few patients have experienced adverse drug reactions with dornase alfa that have required permanent discontinuation of the treatment.
2. **Pregnancy and Breast Feeding** - The safety of dornase alfa has not been established in pregnant women. There is minimal systemic absorption of dornase alfa and therefore no measurable concentrations of dornase alfa would be expected in human milk. Advising patients who are pregnant or breastfeeding is the responsibility of the CF Consultant.

Clinically Significant Drug Interactions (refer to BNF for a full list)

- No clinically significant drug interactions

Colistimethate Sodium (Promixin® Powder for Nebuliser Solution OR Colomycin® Injection)

Dose, Route of Administration and Duration of Treatment	Monitoring Undertaken by Specialist Requesting Shared Care	Ongoing Monitoring to be Undertaken by GP	Stopping Criteria	Follow Up
Promixin® Colistimethate sodium 1 million units nebulised twice daily via I-neb® nebuliser. Each vial requires reconstitution with 1ml of Water for Injection or 1ml of 0.9% Sodium chloride prior to use **Colomycin®** Colistimethate sodium 1 or 2 million units nebulised twice daily. (reconstitution instructions : Each vial requires reconstitution with 4ml of Water for Injection or Sodium Chloride 0.9% prior to use) Occasionally the vials may be reconstituted with 2ml of salbutamol 5mg nebules and 2mls of water for injection or sodium chloride if it is felt beneficial to the patient, this will be established during their test dose of colistimethate sodium) **Duration of treatment** Eradication of Pseudomonas aeruginosa – 3 months (may be repeated if unsuccessful) Treatment of chronic pseudomonas aeruginosa colonisation – Indefinite	**Baseline** Lung function (FEV_1) taken pre and post first test dose to check for excessive bronchoconstriction and/or wheeze to ensure suitability of the drug Oxygen saturations, Renal function and sputum microbiology culture and sensitivities **At 1 and 3 months** Lung function (FEV_1), sputum microbiology culture and sensitivities and renal function	No routine monitoring is necessary Refer to the CF team if nephrotoxicity is identified by GP Report any concerns about side-effects, pregnancy, overuse or lack of efficacy to the CF team. Report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk	No changes should be made to treatment without prior discussion with the CF team; if a rash develops please discuss with CF team as soon as possible Intolerable adverse effects would necessitate withdrawal Colistimethate sodium has not been shown to improve lung functions in studies therefore if there is a continued loss of lung function (more than 1% per year) alternative antibiotics should be considered (but may also be used in addition to colistimethate sodium).	**Specialist** Patients monitored 3 monthly - Lung function (FEV_1), weight, oxygen saturation and symptoms Send a letter/results notification to the GP after each clinic attendance Advise GP on review, duration and/or discontinuation of treatment where necessary **GP** To follow up as required at discretion of GP Request patient seen earlier if adverse effects experienced between appointments

Colistimethate Sodium (cont)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to BNF for full list)

1. **Adverse effects** – Cough, chest tightness, bronchoconstriction/bronchospasm, rash, sore throat and sore mouth
2. **Myasthenia Gravis** – Colistimethate sodium nebuliser solution is known to reduce the amount of acetylcholine released from the pre-synaptic neuromuscular junction and should therefore not be used in patients with myasthenia gravis
3. **Porphyria** – Use with extreme caution in patients with porphyria
4. **Renal impairment** - Colistimethate sodium is renally excreted and is nephrotoxic if high serum concentrations are achieved. Whilst this is unlikely with inhaled therapy, renal function should be monitored.
5. **Pregnancy and Breastfeeding** – The safety of colistimethate sodium nebuliser solution has not been established in pregnant women. Colistimethate sodium is excreted in human milk. Advising patients who are pregnant or breastfeeding is the responsibility of the CF Consultant

Clinically Significant Drug Interactions (refer to BNF for full list)

- **Ciclosporin** (↑ risk of nephrotoxicity – monitor renal function)
- **Neuromuscular blocking drugs, non-depolarising** (avoid - Prolongation of neuromuscular blockade)
- **Loop diuretics** (avoid - ↑ risk of ototoxicity)
- **Neostigmine and Pyridostigmine** (avoid – antagonises effects of neostigmine and pyridostigmine)

Tobramycin (300mg in 4ml or 300mg in 5ml Nebuliser solution)

Dose, Route of Administration and Duration of Treatment	Monitoring Undertaken by Specialist Before Requesting Shared Care	Ongoing Monitoring to be Undertaken by GP	Stopping Criteria	Follow Up
300mg nebulised twice daily for 28 days followed by a 28 day tobramycin free period (during which an alternative antibiotic may be used). The dose interval should be as close as possible to 12 hours and not less than 6 hours **Duration of treatment** Eradication of Pseudomonas aeruginosa – 1-3 months (may be repeated if unsuccessful) This is only to be used if treatment with colistimethate sodium has proven to be unsuccessful Treatment of chronic pseudomonas aeruginosa colonisation - Indefinite	**At initiation:** Baseline lung function (FEV_1) taken pre and post 1st test dose to check for excessive bronchoconstriction and/or wheeze and ensure suitability of drug Oxygen saturations, sputum microbiology culture and sensitivities, renal function and symptoms. **At 1 and 3 months** Lung function (FEV_1), sputum microbiology culture and sensitivities and renal function	No routine monitoring is necessary Refer to CF team if nephrotoxicity, tinnitus, hearing loss or haemoptysis is identified Report any concerns about side-effects, pregnancy, overuse, poor adherence or lack of efficacy to the CF team Report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk	Failure to respond to treatment, deterioration of lung function, adverse effects that necessitate withdrawal. Decisions to permanently stop treatment should be made by the CF team Alternative antibiotics may be used in conjunction with tobramycin nebules on a month on/month off basis **Withhold and discuss with the CF team if any of the following occur** Nephrotoxicity, ototoxicity and haemoptysis	**Specialist** Patients monitored 3 monthly Lung function (FEV_1), weight, oxygen saturation and symptoms Renal function will be checked annually Audiometry will be organised if patient reports tinnitus of hearing loss If tobramycin induced nephrotoxicity/ototoxicity suspected, tobramycin level will be taken, monitored and any necessary adjustments to therapy made Send a letter/results notification to the GP after each clinic attendance Advise GP on review, duration and/or discontinuation of treatment where necessary **GP** To follow up as required at discretion of GP Request patient seen earlier if adverse effects experienced between appointments

Tobramycin (cont)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to BNF for full list)

1. **Adverse effects** - Lung disorder, rhinitis, dysphonia, sputum discoloured, cough, malaise, pulmonary function test decreased, tinnitus, myalgia and laryngitis
2. **Neuromuscular disorders** - Aminoglycosides may aggravate muscle weakness due to a potential curare-like effect on neuromuscular function. Therefore use with great caution in patients with known or suspected neuromuscular disorders such as parkinsonism or other conditions characterised by myasthenia, including myasthenia gravis
3. **Nephrotoxicity and ototoxicity** - If either occurs in a patient receiving nebulised tobramycin, therapy should be discontinued until serum concentration falls below 2 µg/mL
4. **Pregnancy and Breastfeeding** - The safety of nebulised tobramycin has not been established in pregnant women. It is not known to what extent nebulised tobramycin is excreted in human milk. Advising patients who are pregnant or breastfeeding is the responsibility of the CF Consultant.

Clinically Significant Drug Interactions (refer to BNF for full list)

- **Loop Diuretics** (avoid - risk of ototoxicity)
- **Intravenous mannitol** (avoid - risk of ototoxicity)
- **Ciclosporin and tacrolimus** (↑ risk of nephrotoxicity – monitor renal function)
- **Neuromuscular blocking drugs, non-depolarising** (avoid - Prolongation of neuromuscular blockade)
- **Neostigmine and Pyridostigmine** (avoid – antagonises effects of neostigmine and pyridostigmine)
- **Vancomycin** (avoid - risk of ototoxicity and nephrotoxicity)

Aztreonam Lysine

Dose, Route of Administration and Duration of Treatment	Monitoring Undertaken by Specialist Before Requesting Shared Care	Ongoing Monitoring to be Undertaken by GP	Stopping Criteria	Follow Up
75mg nebulised three times a day for 28 days, followed by a 28 day aztreonam lysine free period (during which an alternative nebulised antibiotic will be used). This is licensed for patients aged 6 years and above. The dose interval should be as close as possible to 8 hours and not less than 4 hours **Duration of treatment** Indefinite	**At initiation** Baseline lung function (FEV_1) taken pre and post 1st test dose to check for excessive bronchoconstriction and/or wheeze and ensure suitability of drug Oxygen saturations, sputum microbiology culture and sensitivities, renal function and symptoms. **At 1 and 3 months** Lung function (FEV_1), sputum microbiology culture and sensitivities and renal function	No routine monitoring is necessary Refer to CF team if haemoptysis is identified Report any concerns about side-effects, pregnancy, overuse, or lack of efficacy to the CF team. Report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk	No changes should be made to treatment without prior discussion with the CF team Failure to respond to treatment, deterioration of lung function, or adverse effects would necessitate withdrawal	**Specialist** Patients monitored 3 monthly Lung function (FEV_1), weight, oxygen saturation and symptoms) Renal function will be checked annually. Send a letter/results notification to the GP after each clinic attendance Advise GP on review, duration and/or discontinuation of treatment where necessary **GP** To follow up as required at discretion of GP Request patient seen earlier if adverse effects experienced between appointments

Practical issues including adverse effects, interactions, other relevant advice and information (refer to BNF for full list)

1. **Adverse effects** – Cough, nasal congestion, wheezing dyspnoea, pharyngolaryngeal pain, chest discomfort, rhinorrhoea, haemoptysis, bronchospasm, rash, arthralgia, joint swelling, pyrexia and reduced lung function
2. **Pregnancy and Breastfeeding** - The safety of nebulised aztreonam lysine has not been established in pregnant women. Advising patients in pregnancy is the responsibility of the CF consultant. Following administration of aztreonam for injection, aztreonam is excreted in human milk at very low concentrations. Systemic concentration of aztreonam following inhaled administration of aztreonam lysine is approximately 1% of the concentration resulting from a standard dose of aztreonam for injection. Therefore, and because of low oral absorption, aztreonam exposure in breast-fed infants due to mothers receiving aztreonam lysine is likely to be extremely low. Nebulised aztreonam lysine can be used during breast-feeding.

Clinically Significant Drug Interactions (refer to BNF for full list)

- No clinically significant drug interactions

Evidence Base for treatment and key references

Fuchs JH, Borowitz DS, et al. Effect of aerosolised recombinant human DNase on exacerbations of respiratory symptoms and on pulmonary function in patients with cystic fibrosis. New Engl J Med 1994;331:636-642.

Robinson PJ. Dornase alfa in early cystic fibrosis lung disease. Pediatr Pulmonol 2002;34: 237-41.

Quan JM, Tiddens HA, Sy JP, McKenzie SG, Montgomery MD, Robinson PJ, et al. A two-year randomized, placebo-controlled trial of dornase alfa in young patients with cystic fibrosis with mild lung function abnormalities. The Pulmozyme® Early Intervention Trial Study Group. J Pediatr 2001;139:813– 20.

Hodson ME, McKenzie S, Harms HK, Koch, Mastella G, Navarro J et al. Dornase alfa in the treatment of cystic fibrosis in Europe: A report from the epidemiologic registry of cystic fibrosis. Paediatr pulmonol 2003;36:427-32.

Shah PL, Hodson ME. Dornase alfa. A practical guide to patient selection and drug use in cystic fibrosis. BioDrugs 1997;8:439-45.

Ratjen F, Rietschel E, Kasel D, Schwiertz R, Starke K, Beier H et al. Pharmacokinetics of inhaled colistin in patients with cystic fibrosis. J Antimicrob Chemother 2006;57:306–11

Ryan G, Mukhopadhyay S, Singh M. Nebulised anti-pseudomonal antibiotics for cystic fibrosis. Cochrane Database Syst Rev 2003;Issue 3. Art. No.: CD001021. DOI: 10.1002/14651858.CD001021

Ramsey BW et al. Intermittent administration of inhaled tobramycin in patients with cystic fibrosis. N Eng J Med 1999; 340:23-30

Assael BM et al. Inhaled aztreonam lysine versus inhaled tobramycin in cystic fibrosis: A comparative efficacy trial. J Cyst Fibros 2013; 12 (2): 130-140

Cystic Fibrosis Trust: Antibiotic Treatment For Cystic Fibrosis. Third Edition. May 2009

NHS England Clinical Commissioning Policy: Inhaled Therapy for Adults and Children with Cystic Fibrosis. December 2014

British National Formulary Online September 2019.
https://www.medicinescomplete.com/mc/bnf/current/index.htm (Accessed September 2019)

Summary of Product Characteristics:
Pulmozyme® 2500 U/ 2.5ml, nebuliser solution
http://www.medicines.org.uk/emc/medicine/1723 (Accessed September 2019)

Promixin® 1 million International Units (IU) Powder for Nebuliser Solution
http://www.medicines.org.uk/emc/medicine/13495 (Accessed September 2019)

Colomycin® Injection
https://www.medicines.org.uk/EMC/medicine/1590/SPC/Colomycin+Injection (Accessed September 2019)

Bramitob® 300mg/4ml Nebuliser Solution
https://www.medicines.org.uk/emc/medicine/21427 Last accessed: September 2019

Tobramycin (Tymbrineb) 300mg in 5ml Nebuliser solution
https://www.medicines.org.uk/emc/product/8830/smpc Last Accessed September 2018Cayston® 75mg powder for nebuliser solution
http://www.medicines.org.uk/emc/medicine/22358 (Accessed September 2019)

Patient Information leaflet:
Pulmozyme® 2500 U/ 2.5ml, nebuliser solution
http://www.medicines.org.uk/emc/medicine/16259 (Accessed September 2019)

Promixin® 1 million International Units (IU) Powder for Nebuliser Solution
http://www.medicines.org.uk/emc/PIL.13532.latest.pdf (Accessed September 2019)

Colomycin® Injection 1 million or 2 million International Units Powder for solution for injection, infusion or inhalation
http://www.medicines.org.uk/emc/PIL.13532.latest.pdf (Accessed September 2019)

Bramitob® 300mg/4ml Nebuliser Solution
http://www.medicines.org.uk/emc/medicine/21475 (Accessed September 2019)

Tobramycin (Tymbrineb) 300mg in 5ml Nebuliser solution
https://www.medicines.org.uk/emc/product/8830/pil (Accessed September 2019)

Cayston® 75mg powder for nebuliser solution
http://www.medicines.org.uk/emc/PIL.22346.latest.pdf (Accessed September 2019)

4. COMMUNICATION AND SUPPORT

King's College Hospital switchboard: 0203 299 9000	
Paediatric consultants Dr Cara Bossley Dr Gary Ruiz	**Paediatric CF coordinator** *Tel:* 0203 299 3562 *Email:* shirleyedie@nhs.net
Immediate general advice CF Specialist Nurses	**Paediatric:** 0203 299 3342
Immediate advice out of hours Registrar/doctors	**Paediatric :** Consultant on call *Tel:* 0203 299 9000 Bleep via switchboard
Medication – Prescribing advice, interactions, availability of medicines **Paediatric CF Pharmacist:** Olivia Mina	**Paediatric CF Pharmacist Direct** *Tel:* 0203 299 9000 (Ext 35723) *Email:* olivia.mina@nhs.net

Note: These are the only contact details provided as King's College Hospital NHS Foundation Trust is the only specialist provider of CF services in South East London.