NHS organisation statement template

Thank you for agreeing to give us your views on the technology and the way it should be used in the NHS.

Primary Care Trusts (PCTs) provide a unique perspective on the technology, which is not typically available from the published literature. NICE believes it is important to involve NHS organisations that are responsible for commissioning and delivering care in the NHS in the process of making decisions about how technologies should be used in the NHS.

To help you give your views, we have provided a template. The questions are there as prompts to guide you. You do not have to answer every question. Short, focused answers, giving a PCT perspective on the issues you think the committee needs to consider, are what we need.

About you

Your name: [redacted]

Name of your organisation: Sandwell Primary Care Trust

Please indicate your position in the organisation:

- commissioning services for the PCT in general
- responsible for quality of service delivery in the PCT
- other (please specify) public health lead for individual funding requests

1) What is the expected place of the technology in current practice?
How the condition is currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences in opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Cystic fibrosis (CF) patients have significant morbidity and mortality, as a consequence of both acute and chronic pulmonary complications. This results in progressive lung damage, with an impact on lung function, quality of life and hospital admissions.

The treatment of cystic fibrosis although subject to some local variation has become more standardised with the development of national guidelines (steered by the CF Trust), the collation of data in the national CF database and the development of local networks to evaluate and standardize practice.

Where there is no evidence through head to head comparisons of different treatments (as is the case for many treatments where comparisons have been made only with placebo), then there will be differences of opinion between clinicians as to what current best practice should be.

There are also differences in practice depending on whether clinicians are dealing with children (with milder disease) or adult patients (with more severe disease). This is partly because CF treatment has a treatment burden, which has to be balanced with potential benefits. Cystic fibrosis patients suffer a significant treatment burden which along with the disease itself, impacts on their quality of life.

There is no cure for cystic fibrosis, but a range of approaches are available to help clear secretions, reduce respiratory inflammation and prevent or reduce bacterial growth. The approaches used to treat the condition, include:

- medications for the lung and airways; bronchodilators, antibiotics (oral, intravenous and nebulised), steroids and enzymes which help the mucociliary clearance including DORNase alpha (recombinant human deoxyribonuclease), and 6% or 7% hypertonic saline
- medications for the digestive system; pancreatic enzymes to help digestion, vitamins, nutritional supplements
- other medications; bisphosphonates, vaccinations
- chest physiotherapy, largely centred on airway clearance
- lung transplants for severe cases

DORNAse alpha has been available for 16 years so there is a wealth of clinical experience in its use and is based on a good evidence base[1,2]. It is effective in improving lung disease, reducing frequency of intravenous antibiotics and has nutritional benefits. It also has some reported anti-inflammatory benefits. However, it is nebulised and takes time to administer and it is expensive.

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[1] Jones AP, Wallis C. Dornase alfa for cystic fibrosis. Cochrane Database of Systematic Reviews 2010, Issue 3. Art. No.: CD001127. DOI: 10.1002/14651858.CD001127.pub2.

[2] Wark P, McDonald VM. Nebulised hypertonic saline for cystic fibrosis. Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD001506. DOI: 10.1002/14651858.CD001506.pub3.

6% and 7% hypertonic saline have been used for the last few years. When directly compared with DORNAse alpha it has been shown to be less effective, but has a role as add-on therapy or for those who are already on DORNAse alpha. It is also nebulised.

The scope for the technology appraisal suggests the following comparators:

- inhaled mucolytics (DORNAse), nebulised hypertonic saline and best supportive care, which may include a wide range of inhaled and oral active treatments

Clinical experience is insufficient to determine whether dry powder mannitol will replace any of these treatments or be used alongside them as additional therapy. More long term data would be required to allow the development of local guidelines. Inhaled dry powder mannitol has only been used as part of the phase III trial. It has the potential benefit of being dry powder, so can be administered more quickly.

The place of this technology in the pathway of care (following licensing and NICE approval) will largely be determined by its affordability for PCTs.

2) To what extent and in which population(s) is the technology being used in your local health economy?
- is there variation in how it is being used in your local health economy?
- is it always used within its licensed indications? If not, under what circumstances does this occur?
- what is the impact of the current use of the technology on resources?
- what is the outcome of any evaluations or audits of the use of the technology?
- what is your opinion on the appropriate use of the technology?

This therapy is not currently routinely available or used in Sandwell local health economy.

To date, mannitol has only been used for CF patients in phase III trials. As aridol mannitol has been used for bronchial challenges in lung function testing.

Locally, four patients have continued its use after completion of the trial on a named patient basis with compassionate supply from Pharmaxis pending licensing applications and the NICE guidance. The patients who have found benefit from the treatment have been keen to continue.

Local clinical experts think that DORNAse alpha would be their first choice in patients whose lung function is deteriorating. However, mannitol would be useful as add-on therapy (as an alternative to hypertonic saline) for those who were still not doing well despite DORNAse alpha and as first line therapy if for some reason they did not tolerate DORNAse alpha.

3) Potential impact on the NHS if NICE recommends the technology. What impact would the guidance have on the delivery of care for patients with this condition?

Mannitol, in its inhaled dry powder formulation, reduces the viscosity of respiratory mucus and stimulates cough through inducing hydration in the airway lumen.

If approved, it is expected that mannitol may have a place in the day-to-day treatment of more severe CF pulmonary complications or for those with poor response to existing mucolytic therapies. It is unclear whether it will replace or used in addition to existing treatment such as rhDNase or hypertonic saline.

Improvement in lung function may potentially reduce the requirement for intravenous antibiotics and improve quality of life for patients with CF. This may result in reduced hospital admissions and contacts with health professionals. Although this has not yet been shown for mannitol, one can extrapolate this from the experience with DORNAse alpha.

4) In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional resources (for example, staff, support services, facilities or equipment)?

Inhaled mannitol should be commenced in a specialist CF or secondary care setting. Lung function testing facilities will be needed, as will the capacity for appropriate follow-up.

Shared care agreement could be set up, whereby the primary care provider will undertake the prescription, but the appropriate monitoring is undertaken by the specialist centre. However, GPs may be reluctant to prescribe a new drug for a relatively rare condition. Patient information leaflets may need updating.

Currently, there are shared care arrangements for the prescription of DORNAse. The first month prescription is issued by hospital and repeat prescriptions by GPs. A few GPs have not signed up to the shared care agreement. In these cases, the repeat prescriptions are issued by the hospital and the cost is claimed from PCT. CF care (including DORNAse) is excluded from payment by results tariffs.

The inhaler is described by the manufacturer as easy-to-use, pocket-size and portable. It will be self-administered, so training of patients may be necessary.

No additional resource implications are obvious with this new treatment.

5) Can you estimate the likely budget impact? If this is not possible, please comment on what factors should be considered (for example, costs, and epidemiological and clinical assumptions).

Currently, the cost of inhaled mannitol is not known. An AGM Pharmaxis shareholder report (2009) suggests that the drug cost may be around £8,000 per patient per annum. There is little further detail regarding this estimate and it is assumed to be based on a dose of 400mg BD, which is in line with the dosing used in the two phase III RCTs sponsored by Pharmaxis.

Once daily DORNAse (2.5ml) costs approximately £6,000 per patient per year. DORNAse may be prescribed once or twice daily as a nebulised solution. Nebulised hypertonic saline is inexpensive.

The potential number of cases eligible for treatment for the Sandwell PCT population has been estimated based on known incidence and prevalence figures for cystic fibrosis. Sandwell PCT has a population of around 335,000. It is estimated that there will be approximately two new CF cases each year (CF incidence 1 in 2500 live births). From clinical records from the three CF centres that provide care for Sandwell PCT residents, there are currently 59 CF Sandwell residents.

West Midlands Adult CF centre:	31		
Birmingham Children's Hospital:	20		
	Age groups:	<1 year	3
		1-5yrs	3
		5-10yrs	5
		10-15yrs	4
		15yr-20yr	5
City Hospital:	8 (ages not known)		
Total	59 CF patients		

In the adult CF setting, 75-80% of patients are on DORNAse. In those aged between 5 and 16 years old, 65-70% are on DORNAse. DORNAse is not licensed in children under 5. According to PCT prescribing records (EPACT), the prescribing costs (prescriptions issued by GPs) for DORNAse alpha were:

2008-09	£85000
2009-10	£60000
2010-11 (8 months data only)	£60000

We do not know the prescribing costs for prescriptions issued by hospitals.

Assuming that 80% of CF patients have respiratory symptoms and are suitable for this therapy, we estimate that the annual cost for Sandwell PCT will be approximately £350,000-400,000. This estimate assumes that therapy is added to existing treatments.

From the information available, it is unclear whether inhaled mannitol will be more appropriate for specific CF patient subgroups, based for example on the extent or severity of their lung disease. The treatment cost, dosing and the duration of treatment will need to be clarified before a more ccurate estimate of the PCT budget impact can be made.

If the lung function threshold for prescribing inhaled mannitol is lower (i.e. better lung function), than it is for DORNAse, then patients not currently being prescribed a mucolytic (other than hypertonic saline), may potentially be commenced on inhaled mannitol. This would increase the total number of mucolytic treated patients within the PCT, over and above those on DORNAse.

Should future larger clinical trials demonstrate an additional or synergistic benefit from combining inhaled mannitol and DORNAse, this would affect the budget impact significantly, as the drugs may then be recommended to be used in combination.

Local CF clinicians think CF patients commencing inhaled mannitol and subsequent evaluation may take an extra 1-2 visits, especially if there are issues around tolerability.

6) Would implementing this technology have resource implications for other services (for example, the trade-off between using funds to buy more diabetes nurses versus more insulin pumps, or the loss of funds to other programmes)?

Where there is an additional cost, there is likely to be an opportunity cost. Until the place of mannitol in the CF treatment pathway is clarified it is unclear whether the cost of introduction of this treatment will be offset by the reduction in costs of other treatments (e.g. less antibiotic usage, fewer hospital episodes etc.).

7) Would there be any need for education and training of NHS staff?

Given that inhaled mannitol will be used in a specialist setting, the extent of education and training within the NHS as a whole is not likely to be significant. Departmental education, as a part of professional training and development is likely to cover these needs. Staff will need to be taught how to use the inhaler and how to teach their patients to do so.

8) Other Issues

Please include here any other issues you would like the Appraisal Committee to consider when appraising this technology.

The small trials and the uncertain clinical significance of small benefits from this treatment compared to existing therapies will need careful consideration. The PCT believes that unless a clear case can be made, confirming that this inhaler provides a net benefit compared to alternatives at a reasonable cost, then it should be used in research settings only.

The PCT will look forward to seeing the manufacturer's estimates of cost effectiveness and how these are arrived at in due course.
There is a lack of evidence to suggest that combining inhaled mannitol and the existing mucolytic DORNAse is additive in effect.

To date there is limited evidence demonstrating how improvements in lung function correlate with longer term clinical outcomes and changes in quality of life. There also appear to be some issues around tolerability (both in terms of side effects cough, nausea) and a drop in FEV1 on initial challenge) with significant drop out rates.

We note that trial NCT00446680, is currently in progress and no results are as yet available. This is a phase III double-blind, randomized controlled trial of 340 cystic fibrosis patients, randomized to mannitol 400mg or placebo, with a primary outcome of FEV_1 improvement.

Another trial (NCT00630812), looking at the long term administration of inhaled mannitol was due to be completed in November 2010. This is a 26 week phase III study with 318 patients, preceded by a 26 week open label phase.

These trials both have secondary outcomes, which will be of interest, namely quality of life and cost effectiveness, including hospital and community care costs.