NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Mannitol dry powder for inhalation for the treatment of cystic fibrosis

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Penelope Agent

Name of your organisation: Royal Brompton & Harefield NHS Foundation Trust

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? ☑
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)? ☑ **Lead Physiotherapist at Royal Brompton & Harefield NHS Foundation Trust, and Chair of the National Association of Chartered Physiotherapists in Cystic Fibrosis**
- other? (please specify)

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What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of 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?

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

Cystic Fibrosis care is managed within specialist centres or clinics throughout the UK. It is not routinely managed in district general hospital. In paediatrics, there is a system of shared care – care jointly provided by one larger specialist centre and a number of smaller specialist clinics. In adult, all care is provided by specialist centres. Multi-disciplinary teams are key to the provision of care in CF.

There are nationally agreed standards of care which are produced by the CF Trust in collaboration with a committee of expert professionals. Professionals work closely together both within and between centres. Individual specialist centres may then produce their own local clinical guidelines but throughout the UK these are broadly in agreement across the board.

Mannitol dry powder for inhalation is a mucoactives agent which ultimately enhances the clearance of excess bronchial secretions by reducing the viscosity of the secretions and stimulating cough. Physiotherapists are key to the initial instruction in the use of Mannitol due to their expertise in optimising breathing pattern and inhalation technique. It falls within the same group of medications such as RhDNase (inhaled mucolytic) and hypertonic saline (enhances airway surface liquid and ultimately, cough). Inhalation therapy is a key aspect and challenge in providing optimal care in CF as the primary problem with the majority of patients is difficulty in clearing excess bronchial secretions (sputum).

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The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

Mannitol dry powder for inhalation is part of a group of drugs known as mucoactives or mucolytics. The other two main drugs in this group which are currently available are RhDNase and hypertonic saline. Both of these are nebulised and require ongoing nebuliser equipment, take approx 10mins each to nebulise and RhDNase has to be stored in the fridge. The option of a dry powder mucoactives will be attractive to patients as it is quicker, easily portable or if used in combination with the other two drugs may give enhanced improvements in sputum clearance and lung function. Patients with CF have an extremely high burden of treatment with several nebulised therapies, airway clearance and exercise for physiotherapy, plus oral medications, so anything that is effective but simple to take is a welcome development.

The clinical trials that have been carried out have accurately reflected usual clinical practice as they were carried out in multiple CF centres. Important outcome measures such as lung function, symptoms, quality of life and reduction in pulmonary exacerbations are vital and have been included within the recent studies. Although some patients complained of increased cough in the trials, my physiotherapy expert opinion would be that patients need to be educated on the type and control of cough. It is inevitable that with a medication that increases mucociliary clearance you will experience more cough as this is the only means of expectorating the secretions. Appropriate education regarding cough can be used to reduce patient concerns over cough. The long term benefit of having improved lung function, clearer airways, and a reduction in symptoms should outweigh the slight increase in cough.

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Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

NICE guidance on the use of Mannitol/Bronchitol would assist in the provision of this as part of standard CF care. NHS staff should not need extra training and education as specialist physiotherapists and nurses who work in CF care already have the specialist skills required for optimising inhalation therapy. This would involve ensuring that patients take the inhaler correctly with the optimal breathing pattern and technique. This is standard for any inhaled therapy. The only additional resource would be to carry out an inhalation challenge test with the first dose of the drug, which again is standard for any new inhaled therapy in CF care. This will be carried out by a specialist physiotherapist or nurse usually and is commonplace for many other inhaled therapies.