Colistimethate sodium powder and tobramycin powder for inhalation for the treatment of pseudomonas lung infection in 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:
With thanks to:
[redacted]

Name of your organisation:
Royal College of Paediatrics and Child Health

Are you (tick all that apply):

X 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)?

X 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.)? NHS, see above

X other? (please specify) Royal medical college

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.

The College notes that inhaled antibiotics are currently used in cystic fibrosis (CF) for two main indications: eradication of *Pseudomonas aeruginosa*; and, maintenance therapy for patients with chronic infection. At present these are given only in nebulised form. Current UK guidelines, *Antibiotic treatment for cystic fibrosis* (May 2009), have been produced by the UK Cystic Fibrosis Trust Antibiotic Working Group, published by Cystic Fibrosis Trust; they may be downloaded at http://www.cftrust.org.uk/aboutcf/publications/consensusdoc/Antibiotic_treatment_for_Cystic_Fibrosis.pdf. These are consensus guidelines, based on a thorough review of the evidence, particularly Cochrane reviews.

Two main antibiotics are currently used - nebulised colistin and nebulised tobramycin. Nebulised aztreonam lysine has recently been licensed for adults with CF. There are variations in practice as to which of these antibiotics is used more often in different parts of the UK. The dry powder technology promises to greatly reduce the administration time for the inhaled antibiotic and hence will reduce the therapeutic burden. Young children (<5 years) may struggle to use the dry powder technology, though it will be suitable for older patients. The proposed technology (dry powder inhaled antibiotics) will be used in specialist centres (secondary or tertiary care). Support for the patient will be needed from doctors, specialist nurses and physiotherapists.

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?

We note these medicines are important new developments, and that there are advantages in allowing movement away from some of the complexities of nebulising liquids.

Dry powder inhalation will reduce administration time and hence reduce therapeutic burden. Clinical studies have shown equal efficacy (compared to nebulised formulation) though minor adverse effects (cough) have been troublesome with dry powder.

The most important efficacy outcomes are time to next exacerbation and FEV1. The most important safety outcomes are bronchospasm, cough and haemoptysis. Prior testing, to assess whether individual patients develop bronchospasm with dry powder, would be sensible before prescribing a prolonged course.

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.

The Cochrane systematic review, *Nebulised anti-pseudomonal antibiotics for cystic fibrosis*, is currently being updated to include dry powder formulations.

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)?

No additional resources or training are needed for implementation. Staff are familiar with dry powder technology formulations for other drugs, e.g. bronchodilators.