NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Technology Appraisal

Colistimethate sodium powder for inhaler device for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of colistimethate sodium powder for inhaler device within its licensed indication for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis.

Background

Cystic fibrosis is an inherited condition characterised by abnormal transport of chloride and sodium across the epithelium in all exocrine tissues, leading to thick viscous secretions in the lungs, pancreas, liver, intestine, and reproductive tract, and an increase in the salt content in sweat gland secretions.

Cystic fibrosis has an incidence of 1 in 2500 live births. In 2007, there were 8080 people with cystic fibrosis registered with the Cystic Fibrosis Trust in the UK, and more than half were older than 16 years of age. About 1 in 25 people in the UK of white European decent are carriers of the cystic fibrosis gene. It is much less common in Afro-Caribbean and Asian people. Although cystic fibrosis is a progressive condition, it has an improving prognosis leading to a rapidly increasing number of adult patients with inevitably more severe problems. In 2005, 97 deaths from cystic fibrosis were recorded in England and Wales, of which 56 had pulmonary manifestations.

While cystic fibrosis is a multi system disease, the primary cause of death in people with cystic fibrosis is respiratory failure resulting from chronic pulmonary infection. *Pseudomonas aeruginosa*, is a bacterium which is the most frequent cause of lung infection in early childhood. The length and quality of life for people with cystic fibrosis is thought to be strongly influenced by the success or failure to eradicate *Pseudomonas aeruginosa* in early childhood and by subsequent antibiotic treatment of respiratory infective exacerbations. In 2003, the age-specific prevalence of *Pseudomonas aeruginosa* in pre-school aged children with cystic fibrosis was 9% rising to 32% for 10 to 15 year olds.

Management of *Pseudomonas aeruginosa* lung infection in cystic fibrosis involves treatment with antibiotics to suppress bacterial growth. Current treatment options include the use of inhaled antibiotics (such as nebulised colistimethate sodium or tobramycin) effective against *Pseudomonas aeruginosa*. Inhaled antibiotic therapy may also be combined with oral

antibiotics (such as ciprofloxacin) to eradicate first or intermittent *Pseudomonas aeruginosa* colonisation. Intermittent administration of intravenous anti-pseudomonal antibiotics may also be given for chronic infection.

The technology

Colistimethate sodium powder for inhalation (Colobreathe, Forest Laboratories UK) belongs to the polymixins class of antibacterials and works by disrupting the structure of the bacterial cell membrane, leading to bacterial death. It is active against Gram-negative organisms including *Pseudomonas aeruginosa, Acinetobacter baumanii, and Klebsiella pneumoniae.* It is supplied as hard capsules which are administered using a 'Turbospin' inhaler device.

Colistimethate sodium powder for inhalation does not currently have UK marketing authorisation for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis. It has been studied in a clinical trial in people with *Pseudomonas aeruginosa* lung infection (including colonisation) in cystic fibrosis compared to nebulised tobramycin.

Intervention(s)	Colistimethate sodium powder inhaler (Colobreathe)
Population(s)	People with cystic fibrosis and *Pseudomonas aeruginosa* lung infection (including colonisation)
Comparators	Colistimethate sodium for inhalation with a nebuliser and other nebulised antibiotics effective against *Pseudomonas aeruginosa*
Outcomes	The outcome measures to be considered include: • mortality • lung function • respiratory symptoms • reduction in hospital admissions • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or

	outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If evidence allows, colistimethate sodium resistance of *Pseudomonas aeruginosa* will be considered.
Related NICE recommendations	Related Guidelines: Clinical Guideline No. 69, July 2008, 'Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care'. Review date: July 2011

Questions for consultation

What are the most appropriate antibiotics used for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis? Can they be nebulised?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)