NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Mannitol for the treatment of cystic fibrosis

Draft scope

Remit/Appraisal objective

To appraise the clinical and cost effectiveness of mannitol dry powder for inhalation within its licensed indication for the treatment of cystic fibrosis

Background

Cystic fibrosis (CF) is an inherited disease caused by genetic mutations. It is characterised by abnormal transport of chloride and sodium, leading to thick viscous secretions in the lungs, pancreas, liver, intestine, and reproductive tract and to an increased salt content in sweat gland secretions. Most of the morbidity and mortality is from pulmonary disease, which is characterised by bronchial and bronchiolar obstruction with thick tenacious secretions that are difficult to clear, colonisation by pathogenic bacteria and repeated infections. There is chronic inflammation and progressive lung destruction leading to bronchiectasis, altered pulmonary function, and respiratory failure. In addition to repeated chest infections, symptoms of CF can include a troublesome cough, prolonged diarrhoea and poor weight gain.

CF is the most common life-limiting, autosomal recessively inherited disease in Caucasian populations, with a carrier frequency of 1 in 25 and incidence of 1 in 2,500 live births. There were approximately 270 babies born in 2006 with CF in England and Wales, and it is estimated that CF affects over 8,000 people in the UK. Although CF is a progressive condition, prognosis is improving with the treatments now available and around half of the CF population can expect to live over 38 years of age. In 2005/06 more than half of the UK population with CF were older than 16 years of age. In 2005, 97 deaths from CF were recorded in England and Wales, 56 of those with pulmonary manifestations.

There is no cure for CF. Management of the pulmonary component of CF includes a range of measures to aid clearance of respiratory secretions and to decrease inflammation and bacterial growth in the respiratory tract. This includes regular physiotherapy to clear respiratory secretions. Bronchodilators (short and long acting beta-2 agonists) are used to manage reversible airway obstruction and help clear secretions. Inhaled mucolytics (such as recombinant human deoxyribonuclease [rhDNase]) and nebulised hypertonic saline are used to thin mucus so it can be cleared more easily. Inhaled antibiotics are used to suppress bacterial growth. Other treatments now considered ‘standard treatment’ for many people with CF include ibuprofen (an anti-inflammatory) and azithromycin (an antibiotic which can help preserve lung function).

The technology

Mannitol dry powder for inhalation (Bronchitol, Pharmaxis) is a mucoactive agent that acts by inducing an influx of water into the airway lumen improving hydration of airway secretions, and increasing mucociliary clearance by reducing its viscosity and stimulating cough. Mannitol dry powder is administered by inhalation with a hand-held, breath activated device.

Mannitol does not have a UK marketing authorisation for the treatment of CF. It is currently being studied, alone and in combination with rhDNase, in clinical trials in people aged 6 years and older with CF compared with placebo.

Intervention(s)	Mannitol dry powder for inhalation
Population(s)	People with cystic fibrosis
Comparators	• Inhaled mucolytics: rhDNase • nebulised hypertonic saline • best supportive care (which may include a wide range of inhaled and oral active treatments)
Outcomes	The outcome measures to be considered include: • mortality • lung function • respiratory symptoms • reduction in pulmonary exacerbations • exercise tolerance • 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. Resource use should take account of any reduction in pulmonary exacerbations in both the primary and secondary care settings.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Details of the components of best supportive care should be clearly described. Consideration will be given to people with a disability who may not be able to manipulate inhaler devices.
Related NICE recommendations	None

Questions for consultation

Have the most appropriate comparators for mannitol in the treatment of cystic fibrosis been included in the scope? Is best supportive care appropriately defined?

Have the appropriate outcome measures been included in the scope?

Are there any subgroups of patients 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?

What do you consider to be the relevant clinical outcomes and other potential health related benefits of mannitol in the treatment of cystic fibrosis, particularly when compared with currently used treatment options?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits